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Original Communications

ON THE CHEMISTRY OF OVARIAN CYSTS*

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THIS report is a part of a general study on ovarian tumors. Previous reports¹⁻³ have been concerned with an attempt to correlate the histology of ovarian cysts, particularly that of the lining of the cyst wall, with the hormonal content of the cyst fluid. The present investigation was designed as a similar study of the chemistry of ovarian cyst fluids. It is believed that the study of the chemistry of fluids offers a unique opportunity to study the chemistry of tumors. Since most ovarian tumors are cystic, it is possible to study the chemical constituents of the fluid which is (or is not) in equilibrium with the cells of a definite and specific character which line the cyst cavity or with the fluid which results from their secretion. This is in contrast with the situation existing in a study of the chemistry of solid tumors in which the chemistry is dependent upon the proportions of different types of cells constituting the tumor tissue. Furthermore, in multilocular malignant tumors frequently only certain cyst cavities manifest malignant characteristics. In this type of tumor a parallel study of the fluids from the different cavities might offer an opportunity to observe any chemical difference between the metabolism of benign and malignant cells.

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Since the physical and chemical properties of the fluids vary with the type of cyst, it is believed that a study of the chemistry of the fluids might be of value in the classification of the tumors and in the determination of the conditions governing their development and growth. A study of the electrolyte balance would throw some light on the laws governing the equilibrium between the tumor tissue and the fluid of the cyst. The part played by the secretory activity of the cells lining the cyst cavity might be shown by a study of the protein and carbohydrate constituents, particularly in those types of cysts producing unusual glycoproteins (e.g., "pseudomucin"). Since these glycoproteins occur only rarely in other body fluids they may be of special import in the metabolism of these tumors.

Although work on the chemistry of ovarian cyst fluids is of long standing and dates back to the work of Scherer⁴ on protein constituents reported in 1852, comparatively little has been done using modern techniques. The early investigations were concerned chiefly with the protein constituents, especially the glycoproteins ("pseudomucins"), and with specific gravity and the percentage of solids. Surveys of the field have been reported briefly by Pfannenstiel,⁵ Wells,⁶ and Stolff⁷ and with a few exceptions are essentially complete. Schepetinsky and Kafitin⁸ have determined calcium, potassium, sodium, phosphorus, and chloride, and observed certain deviations in the mineral content which they have attempted to correlate with the type of the tumor. Schalyt⁹ found that the salt content of the fluid of neoplastic cysts was greater than that of the serum of these patients and that the reducing substance was low or absent. Schalyt⁹ concluded that the development of the cyst was dependent upon two factors: namely, the secretory activity of the epithelium and the disturbance in the osmotic equilibrium. Blair-Bell and Datnow¹⁰ have reported qualitative and quantitative data on total solid, water, inorganic matter, total nitrogen, protein, mucin, pseudomucin, cholesterol, sugar, urea, fats, fatty acids and soap. Numerous workers have reported on cholesterol and lipids in ovarian tumors but these have usually been solid tumors.

Our data have been collected in a preliminary study prior to an investigation of the glycoproteins and a study of the membrane equilibrium. Since the work has been discontinued the findings reported here are of necessity of a fragmentary nature. The data include determinations of specific gravity, solid, water, ash, sodium, potassium, chloride, total nitrogen, nonprotein nitrogen, protein and glucose. Sixteen fluids were obtained from benign ovarian cysts, twelve from malignant cysts and one from a tuboovarian cyst. Fluids from three parovarian cysts were examined also.

Description of the Pathologic Material

A specimen of the cyst wall was taken from each cavity from which fluid was obtained for chemical analysis. The various cyst cavities of

the same tumor are designated by different letters. Bilateral tumors appear with brackets in Table I with the exception of the tubo-ovarian cyst No. 343 and parovarian cyst No. 344 which also occurred in the same patient. The tissues were fixed in formalin and stained with hematoxylin and eosin.



Fig. 1.—Cyst No. 341. Simple serous cyst. Low magnification ($\times 120$) showing cyst wall with irregular lining of low cuboidal epithelial cells and an underlying layer which is relatively avascular and hyalinized.

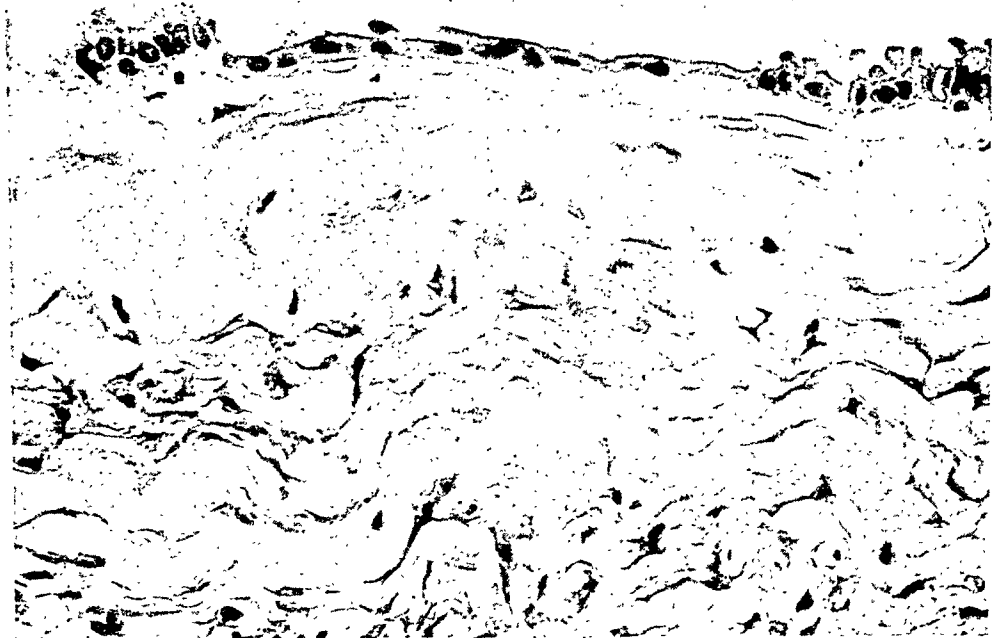


Fig. 2.—Cyst No. 341. Simple serous cyst. High magnification ($\times 370$) from section shown in Fig. 1, showing irregular epithelium and noncellular basal layer. Fluid is low in protein and potassium and high in chloride.

TABLE I. CHEMICAL COMPOSITION OF OVARIAN AND PAROVARIAN CYST FLUIDS

| CYST NO. | TYPE | VOLUME FLUID ML. | % TOTAL SOLID | % WATER | % ASH | MG. PER L. MILLEQUIVALENTS PER LITER | | | | | GRAMS PER LITER | | | |
|----------------------|----------------|------------------|---------------|---------|-------|--------------------------------------|---------|--------|-------------|------------|-----------------|-----------------------|------------------|---------|
| | | | | | | SPECIFIC GRAVITY | GLUCOSE | SODIUM | POTAS- SIUM | CHLO- RIDE | TOTAL NITROGEN | NON- PROTEIN NITROGEN | PROTEIN NITROGEN | PROTEIN |
| BENIGN OVARIAN CYSTS | | | | | | | | | | | | | | |
| 341 | Simple serous | 375 | 1.31 | 98.69 | 1.26 | 1.009 | | 139.9 | 2.82 | 148.6 | 1.34 | 0.15 | 1.19 | 7.4 |
| 356 | Simple serous | 1110 | 0.97 | 99.03 | 1.27 | 1.005 | 30 | 152.2 | 3.16 | 132.4 | 1.76 | 0.12 | 1.64 | 10.3 |
| 337A | Pseudomucinous | 162 | 15.48 | 84.52 | 1.13 | 1.044 | | 153.2 | 5.17 | 87.5 | 21.35 | 0.40 | 20.95 | 130.9 |
| 337B | Pseudomucinous | 268 | 10.98 | 89.02 | 1.18 | 1.034 | | 110.2 | 4.30 | 100.7 | 19.63 | 0.54 | 19.09 | 119.4 |
| 337C | Pseudomucinous | 44.5 | | | | | | | | | 11.61 | | | |
| 337D | Pseudomucinous | 33 | | | | | | 135.7 | 5.04 | 99.1 | 14.71 | | | |
| 337E | Pseudomucinous | 48 | 17.65 | 82.35 | 1.22 | 1.051 | | 127.6 | 5.24 | 92.8 | 23.36 | | | |
| 340 | Pseudomucinous | 1192 | 1.67 | 98.33 | 1.30 | 1.007 | | 146.0 | 4.23 | 148.1 | 0.85 | 0.24 | 0.61 | 3.8 |
| 352 | Pseudomucinous | 4259 | 7.42 | 92.58 | 0.87 | | 1060 | | | 136.4 | 3.45 | 0.51 | 2.94 | 18.4 |
| 358 | Pseudomucinous | 630 | 1.80 | 98.20 | 1.25 | 1.006 | 80 | 137.1 | 3.33 | 143.1 | 1.09 | 0.05 | 1.04 | 6.5 |
| 339A | Granulosa† | 745 | | | | | | 137.1 | | 109.5 | 8.14 | 0.21 | 7.93 | 49.6 |
| 339B | Granulosa | 415 | 6.32 | 93.68 | 1.18 | 1.019 | | 128.8 | 3.05 | 101.9 | 7.53 | 0.21 | 7.32 | 45.8 |
| 339C | Granulosa | 45 | 5.70 | 94.30 | 1.27 | 1.018 | | 152.4 | | 111.6 | 7.23 | 0.19 | 7.04 | 44.0 |
| 339E | Granulosa | 85 | 5.85 | 94.15 | 1.20 | 1.018 | | 138.0 | | 114.7 | 6.99 | 0.22 | 6.77 | 42.3 |
| 339F | Granulosa | 129 | 6.70 | 93.30 | 1.20 | 1.019 | | 139.8 | | 112.4 | 7.46 | 0.23 | 7.23 | 45.2 |
| 349 | Fibro-adenoma | 338 | 5.98 | 94.02 | 1.24 | 1.019 | 270 | 141.5 | 3.46 | 112.9 | 6.47 | 0.37 | 6.10 | 38.1 |
| 343* | Tuboovarian | 50 | 1.56 | 98.44 | 1.64 | | 11 | 155.1 | 3.88 | 131.4 | 0.49 | 0.11 | 0.38 | 2.4 |

| MALIGNANT OVARIAN CYSTOMAS | | | | | | | | | | |
|----------------------------|------|-------|-------|------|-------|-------|-------|-------|------|------|
| | | | | | | | | | | |
| 338A | 5750 | 6.92 | 93.08 | 1.18 | | | | 7.55 | 0.80 | 6.75 |
| 338B | 9 | 11.56 | 88.44 | 0.97 | | | 100.7 | | | 42.3 |
| 338C | 8 | 11.42 | 88.58 | 1.16 | | 131.8 | | | | |
| 338D | 8 | 7.57 | 92.43 | 1.07 | | 117.3 | 95.0 | 12.50 | | |
| 345A | 431 | 6.88 | 93.12 | 1.18 | 1.020 | 250 | 117.3 | 9.04 | 0.22 | 8.82 |
| 345B | 348 | 7.35 | 92.65 | 1.20 | 1.021 | 340 | 117.4 | 6.90 | 0.06 | 55.1 |
| 345C | 166 | 4.86 | 95.14 | 1.25 | 1.015 | 340 | 109.1 | 5.69 | 0.15 | 42.8 |
| 345D | 199 | 7.61 | 92.39 | 1.19 | 1.022 | 140 | 109.5 | 9.78 | 0.12 | 34.6 |
| 346A | 141 | 6.64 | 93.36 | 1.20 | 1.020 | 90 | 115.3 | 8.24 | 0.19 | 60.4 |
| 351 | 190 | 8.71 | 91.29 | 0.53 | 1.024 | 90 | 107.1 | 2.19 | 0.35 | 50.4 |
| 353 | 15 | | | | | 580 | 109.3 | 13.60 | | 11.5 |
| 354A | 79.5 | 8.95 | 91.05 | 1.14 | 1.024 | 60 | 110.6 | 4.06 | 0.37 | 3.69 |
| PAROVARIAN CYSTS | | | | | | | | | | |
| 344* | 88 | 1.58 | 98.42 | 1.58 | 1.006 | 35 | 127.5 | 0.92 | 0.16 | 0.76 |
| 348 | 1537 | 1.00 | 99.00 | 1.24 | 1.004 | 140 | 127.5 | 0.26 | 0.13 | 4.8 |
| 350 | 782 | 1.02 | 98.98 | 0.92 | 1.004 | 160 | 126.5 | 0.21 | 0.10 | 0.8 |
| | | | | | | | | | | 0.7 |

*Cysts 443 and 444 occurred in the same patient.

Braces denote bilateral tumors.

†Fluids except from locule B had a trace of blood.

The series consists of 2 simple serous cysts, 4 pseudomucinous cysts, 1 granulosa-cell tumor associated with an arrhenoblastoma, 1 cystic fibro-adenoma, 2 bilateral malignant and 2 unilateral malignant cystomas, 3 parovarian cysts and 1 tuboovarian cyst.

Brief descriptions of the microscopic findings are listed as they appear in Table I.

CYST No. 341.—Simple serous cyst. (Figs. 1 and 2.) The lining of the cyst cavity consists of an irregular layer of low, cuboidal epithelial cells with little cytoplasm and shows evidence of degeneration. The layer underlying the lining is relatively avascular and hyalinized connective tissue.

CYST No. 356.—Simple serous cyst. The cyst cavity is lined with single layer of low cuboidal epithelial cells consisting chiefly of chromatin and apparently not functionally active. The underlying layer is composed mostly of fibrous tissue showing some hyalinization.

CYST No. 337.—Pseudomucinous cyst. *A.* (Figs. 3 and 4.) The lining of cyst cavity shows marked secretory activity and proliferation which is atypical in some areas and suggests malignant tendencies. The epithelial cells vary, but are mucus-containing and tall columnar in type. The wall is quite cellular and vascular and contains numerous fibroblasts.

B. The cyst wall is essentially the same as *A* but shows less papillary growth and has a slightly less dense underlying layer.

C. This cyst wall is essentially the same as *A* and *B*, but shows a more orderly arrangement and more secretory activity with numerous cells of type shown on the right of Figs. 3 and 4.

D. The cyst lining is similar to *A* but the underlying layer is composed of innumerable locules lined with regular tall columnar cells with basal nuclei. The cells are actively secreting. The fibrous tissue between the locules is quite vascular and very cellular.

E. The cyst lining is of cuboidal epithelium but the wall is denuded in most areas. Otherwise it is similar to *D* but the lining of locules is less active and more degenerate. The underlying layer is loosely fibrous and avascular but with some dense portions.

CYST No. 340.—Pseudomucinous cyst. (Figs. 5 and 6.) The cyst is lined with a regular layer of columnar epithelial cells with basal nuclei with some tendency toward papillary growth. The cells are less actively proliferating than in Cyst No. 337. The underlying layer is not cellular; is relatively avascular, and shows some hyalinization.

CYST No. 352.—Pseudomucinous cyst. The cyst is lined with regular layer of very tall columnar cells with basal nuclei. It is similar to Cyst No. 340 but with locules in the basal area, and slight tendency to papillary formation. The underlying layer is not cellular and is less hyalinized than Cyst No. 340.

CYST No. 358.—Pseudomucinous cyst. The cyst is lined with high columnar cells showing secretory activity or is devoid of epithelium. The underlying layer is quite vascular and cellular in some areas but is hyalinized and not cellular in areas which are denuded.

CYST No. 339.—Granulosa-cell tumor with probable association with an arrhenoblastoma. *A.* There is no distinct cyst wall. The cells are masses of chromatin with very little cytoplasm and the masses of cells are interspersed with fibrous tissue. The stroma is quite vascular. The underlying tissue is a fibrous layer abundantly supplied with tissue



Fig. 3.—Cyst No. 337A. Pseudomucinous cyst. Low magnification ($\times 120$) of two portions of the same cyst wall showing tall columnar epithelium and cellular underlying layer.

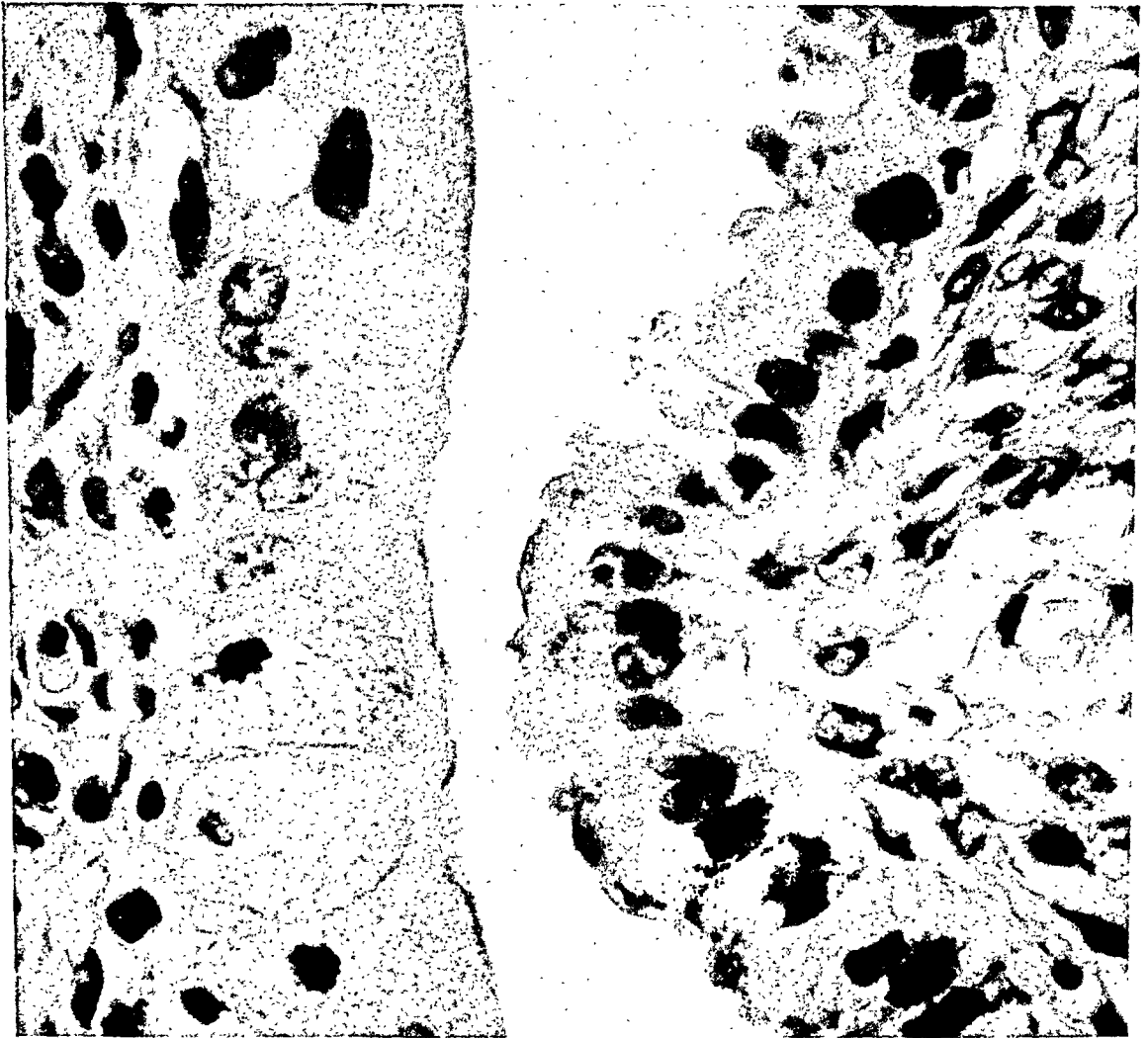


Fig. 4.—Cyst No. 337A. Pseudomucinous cyst. High magnification ($\times 450$) of two parts of same cyst wall shown in Fig. 3. Epithelial cells are actively secreting and the underlying layer is cellular. Fluid is high in protein and potassium and low in chloride.

fluids. The outer wall is fibrous and shows evidence of hyaline degeneration.

B. Same as *A.* Granulosa-cell tumor.

C. The cyst wall is thin and devoid of epithelium in most areas. The superficial layer is densely cellular, fibrous tissue underlaid with fibrous tissue with numerous blood vessels.



Fig. 5.—Cyst No. 340. Pseudomucinous cyst. Low magnification ($\times 120$) showing regular cyst lining of tall columnar epithelium and an underlying layer which is noncellular.



Fig. 6.—Cyst No. 340. Pseudomucinous cyst. High magnification ($\times 450$) of the cyst wall shown in Fig. 5. Cells are less actively secreting than those in Cyst No. 337A and the underlying layer is noncellular. The protein is low and the potassium and chloride are high.

E. The cyst wall is densely cellular and the microscopic section resembles those of cysts *A*, *B* and *C*.

F. This wall is devoid of epithelium and shows considerable hemorrhage and hyalinization.

CYST No. 349.—Cystic fibro-adenoma. The cyst wall is lined by a single layer of epithelial cells which are chiefly deep-staining nuclear tissue with very little cytoplasm. In some areas the underlying tissue is cellular and in others, it is avascular and hyalinized.

CYST No. 343.—Tuboovarian cyst. (See also Cyst No. 344 from the same patient.) The cyst wall is lined by an attenuated layer of cuboidal epithelial cells with very little cytoplasm and shows evidence of degenerative change. The underlying layer is loosely fibrous connective tissue showing hyaline changes.

CYST No. 338.—Malignant pseudomucinous cystoma. *A.* The wall is devoid of epithelial cells except for several scattered cells. The underlying layer shows hyaline degeneration and the wall is fibrous. This section shows no evidence of malignancy.

B, *C* and *D* are sections through the area containing small locules *B*, *C*, and *D*. The cyst walls are lined with regular layer of tall columnar epithelium showing some functional activity. The underlying layer is not cellular, and is fibrous with a tendency toward hyalinization. There is no evidence of malignancy.

A section through the solid portion of the tumor shows the malignant character of tumor.

Cyst No. 345 and Cyst No. 346 are bilateral tumors.

CYST No. 345.—Malignant papillary serous cystoma. *A.* The cyst is lined by irregularly proliferating low cuboidal cells which are poorly preserved and contain little cytoplasm. The underlying fibrous layer is well preserved and vascular. This is a malignant tumor.

B. The cyst is lined by atypical cells with a moderate amount of cytoplasm and shows active proliferation and papillary ingrowths. The underlying layer is cellular and the connective tissue is well preserved and reasonably vascular. This is a malignant tumor.

C. This section is similar to *B* but with glandlike structures lined by proliferating cells; some regions are lined by a single layer of epithelial cells. The underlying layer is cellular in some areas and shows hyalinization in others.

D. This cyst wall is similar to *B* with numerous papillary projections of actively proliferating atypical cells of a malignant character. The stroma is vascular and well preserved.

CYST No. 346A.—Malignant papillary serous cystoma. This cyst wall is similar to Cyst No. 345 *B* and *D*.

CYST No. 351.—Malignant serous cystoma. The cyst wall is devoid of epithelium in most areas, hyalinized and contains islands of adenocarcinoma cells.

Cyst No. 353 and Cyst No. 354 are bilateral malignant cystomas.

CYST No. 353.—The epithelial lining is proliferating atypically with a tendency toward papillary growth. The connective tissue layer is fairly well preserved. The tumor is malignant.

CYST No. 354 *A.*—Cyst wall is composed chiefly of proliferating cells with marked papillary growth and little stroma. The connective tissue is well preserved.

Cyst No. 344.—Parovarian cyst. (See also Cyst No. 343 occurring in the same patient.) The cyst wall is lined with a single layer of epithelial cells of cuboidal type showing some cytoplasm and slight secretory activity. There is some tendency toward papillary development with fairly normal connective tissue and vascularity but also some hyaline change. The underlying layer is not cellular.

Cyst No. 348.—Parovarian cyst. The cyst wall shows marked degeneration and is lined with epithelial cells which consist almost entirely of chromatin. The lining is lost in some areas and attenuated in others. Connective tissue is slightly vascular and shows definite hyalinization.

Cyst No. 350.—Parovarian cyst. The cyst was lined with epithelial cells which are chiefly chromatin and tend to be in more than one layer. There are some papillary tendencies. The tissue of the wall is mostly fibrous and relatively avascular.

Chemical Methods

General: The cysts were received directly from the operating room and the fluid aspirated from each cyst cavity as quickly as possible to prevent diffusion of the chemical constituents due to changes in membrane equilibrium. A specimen of tissue was taken from the wall of each cyst from which fluid was obtained for analysis. The various fluids obtained from the different locules of the same tumor are designated by different letters. Unless otherwise designated the fluids analyzed were free from blood macroscopically. Fluids were centrifuged immediately to remove any sediment. Analyses were made in duplicate or triplicate.

Specific gravity was determined at room temperature, 24 to 26° C., using calibrated 2 or 5 ml. specific gravity bottles.

Total solid and water were determined from weighed samples dried to constant weight at 100 to 107° C., using 2 to 5 ml. of fluid.

Ash was determined on the dried sample obtained from the total solid determination. The dried sample was ignited in a muffle furnace at 475 to 500° C., for 2 hours. It was cooled and moistened with concentrated nitric acid, heated at 475 to 500° C. for 2 hours and the ash weighed. This was repeated once or twice.

Sodium was determined by the method of Butler and Tuthill.¹¹

Potassium was determined by a method based on the procedures of Shohl and Bennett¹² and Consolazio and Talbott,¹³ as follows:

One milliliter of cyst fluid and 0.6 ml. 4N H₂SO₄ were heated in an oven at 100 to 107° C. in a silica crucible until charred. The crucible was placed in a cool furnace, the temperature raised gradually and maintained at 450 to 500° C., until the ash was white or nearly so. Three-tenths of a milliliter of chloroplatinic acid (10 per cent platinum) and 1 drop of 1N HCl were added to the cooled ash. After adding 5 ml. 95 per cent ethyl alcohol the crucible was placed in the refrigerator for 20 minutes. The precipitate was then transferred to a 50 ml. conical centrifuge tube by washing with portions of 95 per cent ethyl alcohol saturated with K₂PtCl₆. The precipitate was centrifuged and the washing discarded. The precipitate was triturated with 95 per cent alcohol saturated with K₂PtCl₆ and centrifuged again; this procedure was repeated. The precipitate was triturated with 10 per cent KCl solution saturated with K₂PtCl₆, centrifuged and the washing dis-

carded. The tube was placed in a water bath at 65 to 75° C., the bath raised gradually to boiling temperature and the heating continued until the precipitate was thoroughly dry and no trace of alcohol remained. Two milliliters of water were added and the tube warmed until solution was complete; 2 ml. 2N KI solution were added and the solution heated for 5 minutes and then titrated immediately with 0.01 N sodium thiosulfate.

Chloride was determined by the Van Slyke¹⁴ method using the Wilson and Ball¹⁵ modification.

Protein-free filtrates were obtained by the cadmium hydroxide precipitation method of Fujita and Iwatake.¹⁶ Filtrates were made immediately. Protein was often precipitated with great difficulty from the pseudomucinous cyst fluids. It was occasionally necessary to alter the proportions of the reagents before complete precipitation was attained. Similar difficulty was observed using the tungstate method.

Total nitrogen was determined by the micro Kjeldahl method employing the Pregl technique¹⁷ but using selenium as the catalyst. Fluids were diluted when the nitrogen value was high.

Nonprotein nitrogen was determined on the protein-free filtrate described above using the Pregl micro Kjeldahl technique.

Protein was calculated from the total nitrogen value, corrected for the nonprotein nitrogen, by multiplying by the factor 6.25.

Glucose was determined by the microtitration method of Miller and Van Slyke¹⁸ using either the micro- or the macro-precipitation method.

Chemistry of Ovarian Cyst Fluids

The data on the chemical analyses of the cyst fluids appear in Table I. It is regrettable that there are not parallel values for the sera of these patients. Although the series is small and the data are incomplete and definite conclusions cannot be drawn, a few variations can be noted.

The *specific gravity* of the ovarian cyst fluids ranges from 1.005 for a simple serous fluid (Cyst No. 356) to 1.051 for a pseudomucinous cyst fluid (Cyst No. 337E). The values for *total solid* range from 0.97 per cent in a fluid of a simple serous cyst (Cyst No. 356) to 17.65 per cent in a pseudomucinous cyst (Cyst No. 337E). Fluids of malignant cystomas are uniformly high (4.86 to 11.56 per cent). The *water* content ranges from 82.4 per cent to 99.0 per cent. The percentage of *ash* is about 1.2 per cent, irrespective of the type of fluid or whether or not the cyst is benign or malignant. The tuboovarian cyst fluid resembled the fluid of the simple serous cysts and parovarian cysts except for a higher ash content. In general, the values are in agreement with those previously reported.

Glucose was determined by the micromethod of Miller and Van Slyke¹⁸ in which protein-free filtrates are obtained by the method of Fujita and Iwatake¹⁶ using cadmium hydroxide as the protein precipitant. According to Miller and Van Slyke, who confirm the work of Fujita and Iwatake, the blood filtrates do not contain more than 1.5 mg. per cent nonfermentable reducing substance. The glucose values are low compared with serum. In this respect the fluids differ from transudates. If there was any hyperglycemic effect due to anesthesia,¹⁹ it did not affect the cyst fluids markedly. The values are in general agreement with those of Schalyt,⁹ but Blair-Bell and Datnow¹⁰ reported nega-

tive results for sugar. However, in retention cysts of the ovary, Schalyt⁹ found normal glucose values but Stolfi⁷ found that 3 of 8 fluids were low. Since tissue membranes are considered permeable to glucose these low values can scarcely be attributed to lack of permeability of the cyst wall. A similar situation exists in synovial fluid in which certain fluids have low glucose values. Allisson and co-workers¹⁹ found glucose values higher in noninfected than in infected synovial fluid; Cajori and Pemberton²⁰ working with sterile fluids found low values when the leucocyte count was high and gave experimental evidence to support the view that the low values were due to glycolysis. Bacteriologic examinations and leucocyte counts were not made in our series but there were no evidences of inflammation. On the other hand, one might be led to consider the possible glycolytic effect of tumor tissue.

The concentrations of electrolytes vary greatly and differ from those commonly accepted for serum. Sodium ranges from 110.2 meq. (milliequivalents*) per liter in locule B of pseudomucinous Cyst No. 337 to 153.2 meq. in Cyst No. 337A. Seventeen of the twenty-five values (68 per cent) fall above and eight fall below the value for serum²¹ (135.1 meq. per liter). A range of ± 5 per cent of this value included 64 per cent of the values; 80 per cent of the values of the fluids of the malignant tumors are in this group and only 53.3 per cent of the values of the benign tumors. Potassium values range from 2.82 to 5.41 meq. per liter. Seventy-six and five-tenths per cent (13 of 17 values) fall below the average value for serum²¹ (4.55 meq. per liter) and 64.7 per cent of the values are more than 5 per cent lower than the value for serum. Chloride values range from 87.5 to 148.6 meq. per liter. Seventy-three and one-tenth per cent of the values exceed the value for serum²² (102.5 meq. per liter); 69.2 per cent exceed the value by more than 5 per cent and 42.3 per cent by more than 10 per cent. This later group includes 50 per cent of the fluids of the benign cysts and 30 per cent of those of the malignant tumors. Six of the 16 fluids of the benign tumors are more than 20 per cent above the value for serum but no fluid from a malignant tumor is above that value. The high chloride values are associated with low protein values. Schepetinsky and Kaftin⁸ reported no appreciable deviation in sodium and chloride but found that the potassium values were low in fluids of serous cysts and higher in pseudomucinous cysts in comparison with the serum of these patients. Schalyt⁹ reported that the salt content was higher in neoplasms than in serum but the same or slightly higher in retention cysts; Stolfi⁷ noted the high salt content of retention cysts.

Total nitrogen varies extremely, from 0.49 grams per liter in tubo-ovarian Cyst No. 343 to 23.36 grams per liter in locule E of pseudomucinous Cyst No. 337. The fluids of the two serous cysts are very low in nitrogen but the fluids of two pseudomucinous cysts are also low. Fluids of pseudomucinous Cyst No. 337 and of two cystadenocarcinomas, Cyst No. 338D and Cyst No. 353, contain more nitrogen than serum and several others approach that value. Nonprotein nitrogen values vary from 0.05 to 0.80 grams per liter. Fifty per cent of the values are more than 20 per cent below and 31.8 per cent are more than 20 per cent above the average value for serum (0.28 grams per liter). These low values may be due chiefly to the use of cadmium hydroxide as the protein precipitant. Protein varies from 2.4 to 130.9 grams per liter.

*The use of the term "milliequivalent" in expressing electrolyte concentration is discussed in J. A. M. A. 115: 1041, 1940.

Chemistry of the Parovarian Cyst Fluids

The data on the chemical analysis of the fluids of parovarian cysts appear in Table I. The specific gravity and the total solid values are low but the values for the ash are not uniform. The low glucose values are in agreement with the findings of Dierks and Becker²³ who found low values and with Stolfi⁷ who reported low values in 4 of 8 fluids, but not with the negative findings of Blair-Bell and Datnow.¹⁰ Sodium values are about the same as for serum but the potassium content is low and the chloride concentration high. The nitrogen and protein content is much lower than in ovarian cyst fluids and the N.P.N. value is also low. In general, the values agree with those previously reported by Dierks and Becker²³ although Stolfi⁷ reported N.P.N. values corresponding to those of serum. The values resemble those of simple serous cysts and other cysts which are not actively secreting.

The Relation of the Chemistry of the Cyst Fluid to the Histology of the Tumor

Not only do the fluids of different types of cysts vary in their chemical composition, but fluids of the same type or even of the different locules of the same tumor differ. In general, the chemistry of the fluid seems to be related to the secretory activity of the epithelial lining of the cyst wall and the basal underlying layer. Those cysts showing marked secretory activity or having an underlying cellular layer have fluids with high protein, low chloride and high potassium; those with less actively secreting epithelium, and showing an avascular or hyalinized basal layer, have fluids which are low in total solid and protein, high in chloride and low in potassium. Cysts in which the wall is denuded or attenuated are also of this type. Except for the higher protein content these fluids resemble transudates in type.²⁴ When the wall of the cyst is secretory in type, the composition of the fluid depends not only upon the osmotic equilibrium, but also upon the activity of the epithelial cells. This is a complicating factor because the electrolyte pattern, according to Donnan's equilibrium, is governed not only by the concentration of the electrolytes but also by the amounts of the nondiffusible substances, such as proteins, which are being produced by the cells of the lining.²⁵ The amount of protein present may depend not only upon the secretory activity of the cyst lining, but also upon the fact that the permeability of a membrane to blood proteins may be altered by a variety of circumstances. The final equilibrium will be subject to the factor of hydrostatic pressure.

That the chemistry of the cyst fluid is related to the character of the tumor is illustrated by two pseudomucinous Cysts, No. 337A and No. 340. Cyst No. 337A (Figs. 3 and 4) has a cyst cavity lined with proliferating epithelial cells with marked secretory activity; the underlying layer has numerous fibroblasts and is quite cellular and vascular. The fluid was high in protein and low in chloride. Cyst No. 340 (Figs.

5 and 6) has a regular lining of epithelial cells showing little evidence of secretory activity and essentially no tendencies toward papillary growth; the underlying layer is relatively avascular and hyalinized. In spite of the pseudomucinous type of the cyst and mucus-containing cells, the fluid is low in nitrogen and protein and high in chloride. Cyst No. 358 is similar to Cyst No. 340 but the wall shows less hyalinization and there is more activity in the cells of the lining. The chloride is lower and the protein is higher than in Cyst No. 340 but the chloride is not as low or the protein as high as in the very actively proliferating Cyst No. 337A. The cyst wall of simple serous Cyst No. 341 (Figs. 1 and 2) shows an irregular lining of low cuboidal cells with little cytoplasm but some degenerative change; the underlying layer is avascular and hyalinized. The fluid is low in protein and potassium and high in chloride. There is a close resemblance between this type of cyst and parovarian cysts both in the histology of the cyst wall and the chemistry of the cyst fluid. The fluids of parovarian cysts are also low in nitrogen and potassium and high in chloride.

Summary and Conclusions

Determinations of sodium, potassium, chloride, nitrogen, nonprotein nitrogen, protein, glucose, total solid, water, ash and specific gravity have been made on 29 ovarian cyst fluids from 15 ovarian tumors (9 benign and 6 malignant); three fluids from parovarian cysts have been examined. Values vary greatly not only among the fluids of different types of cysts, but also between the fluids of the different cavities of the same tumor. The findings are correlated with the histology of the tumor. The composition of the fluid seems to vary with the secretory activity of the lining of the cyst. In general, fluids from cysts with actively secreting epithelium and a cellular basal layer are high in nitrogen and protein, high in potassium and low in chloride; those with less actively secreting epithelium, or a cyst wall which is denuded or attenuated, and in which the basal layer is avascular or hyalinized show low nitrogen and protein, low potassium and high chloride.

We wish to express our appreciation to the members of the staff who have made the clinical material available.

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CESAREAN SECTION MORBIDITY AND SEPTIC MORTALITY IN RELATION TO THE TYPE OF OPERATION*

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PREVIOUS reviews of cesarean sections show that the death rate from this procedure drops sharply as the percentage of elective operations increases. When the operation follows a period of labor, however, there is an increase in deaths commensurate with the duration of labor. Septic infection, notably peritonitis, holds an unenviable position as chief of the causes of death following abdominal delivery, accounting for 36.3 per cent of the deaths in Philadelphia in 1941. We¹ have reported elsewhere that the Philadelphia Maternal Mortality Committee deemed preventable nearly one-third of the septic cesarean deaths occurring in the years 1931 to 1940 inclusive because the operation followed prolonged labor. The results of a questionnaire sent to Philadelphia hospitals in 1940 by Schumann² showed that 4.2 per cent of the sections performed in that year were of the "neglected dystocia" variety. Realizing that even now a woman dies in this city from post-cesarean sepsis every five weeks and that more than a third of the operations still are accomplished after a period of labor, in fifteen per cent of which the membranes are ruptured and prior vaginal examination performed, it would seem fitting to review this problem from the standpoint of morbidity and mortality in relation to the type of operation.

A voluminous literature discloses debates, sometimes acrimonious, concerning the merits of the various types of cesarean section. In the discussion following a report by Lull³ on cesarean sections in Philadelphia in 1931 and 1941 respectively, it was generally agreed that there was little need for the extraperitoneal operation as advocated by Waters, Burns, Aldridge, Ricci and others. Gustafson⁴ in a recent review of transverse cervical sections concludes that the extraperitoneal approach would have offered no increased protection to his patients and states that the Porro operation is the procedure of choice when actual infection exists. In their reports Fall⁵ and Ryder⁶ cast doubt on the superiority of the low segment operation. At the Philadelphia Lying-in Hospital there is no routine operation. A majority of the staff prefers the classical operation for the patient not in labor, reserving the Kerr cervical section for the patient in labor or with ruptured membranes and the Waters or Porro operation for the infected patient.

It is reasonable to propose that a woman can rarely die of sepsis unless the postoperative course has been morbid. To determine the current

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relationship of the type of operation to morbidity, we have reviewed all cesarean sections performed at the Philadelphia Lying-in Hospital during the past three years. The gross morbidity is expressed according to the standard of the American Committee on Maternal Welfare. During this period there have been four hundred and nine cesarean sections performed by twenty-nine operators with three deaths or 0.7 per cent. Distribution of the operations by type is shown in Table I.

TABLE I. DISTRIBUTION OF OPERATIONS BY TYPE

| | NUMBER | PERCENTAGE IN LABOR |
|-----------|-----------|---------------------|
| Classical | 286—69.9% | 10.1 |
| Low | 103—25.2% | 53.3 |
| Porro | 15—3.7% | 26.6 |
| Waters | 5—1.2% | 100.0 |

In comparing the results of the classical and low operations we find that ninety per cent of the patients having a classical section were operated upon before labor began with a total morbidity of 25.5 per cent compared to 28.1 per cent for the low operation, 53.3 per cent of whom were in labor. Table II shows that the low section is followed by much lower morbidity except in the group in labor under twelve hours.

TABLE II. MORBIDITY IN RELATION TO THE DURATION OF LABOR

| HOURS OF LABOR | CLASSICAL | | LOW | |
|---------------------|-----------|----------|--------|----------|
| | NUMBER | % MORBID | NUMBER | % MORBID |
| 0 | 256 | 23.3 | 48 | 12.5 |
| 0 to 12 | 23 | 30.4 | 24 | 33.3 |
| 12 to 24 | 4 | 100.0 | 22 | 45.4 |
| 24 plus | 2 | 100.0 | 9 | 55.5 |
| Average days morbid | 3.5 | | 4.1 | |

However, in this group the duration of labor in the low sections generally approached twelve hours, while most of the classical sections were performed after less than three hours of labor. It is noteworthy that six patients, all morbid, had classic operations after more than twelve hours of labor. One of these also had ruptured membranes for sixty hours, was severely infected and was hospitalized seventy-four days.

If the membranes were ruptured (Table III) the percentage of morbidity rose and again the low operation shows a more favorable rate.

TABLE III. MORBIDITY IN RELATION TO RUPTURED MEMBRANES

| DURATION | CLASSICAL | | LOW | |
|----------|-----------|----------|--------|----------|
| | NUMBER | % MORBID | NUMBER | % MORBID |
| 0 | 275 | 24.0 | 67 | 19.4 |
| 0 to 12 | 6 | 33.3 | 21 | 42.7 |
| 12 plus | 4 | 100.0 | 15 | 46.6 |

If labor had progressed until there was a temperature elevation, the morbidity was 60 per cent in the fifteen low sections and 100 per cent

in the five classical operations exhibiting this complication. The morbidity rate in two hundred and fifty-eight elective classical sections with unruptured membranes was 23.2 per cent in contrast to 9.5 per cent in forty-two similar low operations. On the other hand when there had been labor for twelve hours with ruptured membranes, 55 per cent of the low sections were morbid in comparison to 100 per cent of the classical. A single vaginal examination preceded the classical operation in fourteen instances while the increase was 250 per cent before the low operation, some patients having had as many as three examinations.

We have favored the use of continuous caudal and low dose, continuous spinal anesthesia in the absence of placenta previa, shock or severe anemia. A comparison (Table IV) of the morbidity rates shows a very minor improvement in elective cases but the postoperative condition of the patient and the uterine tone is vastly improved under block anesthesia.

TABLE IV. MORBIDITY IN RELATION TO ANESTHESIA
(No Labor and With Intact Membranes)

| | CLASSICAL | | LOW | |
|--|-----------|----------|--------|----------|
| | NUMBER | % MORBID | NUMBER | % MORBID |
| Continuous spinal and Continuous caudal | 67 | 22.3 | 22 | 9.0 |
| General | 191 | 23.5 | 20 | 10.0 |

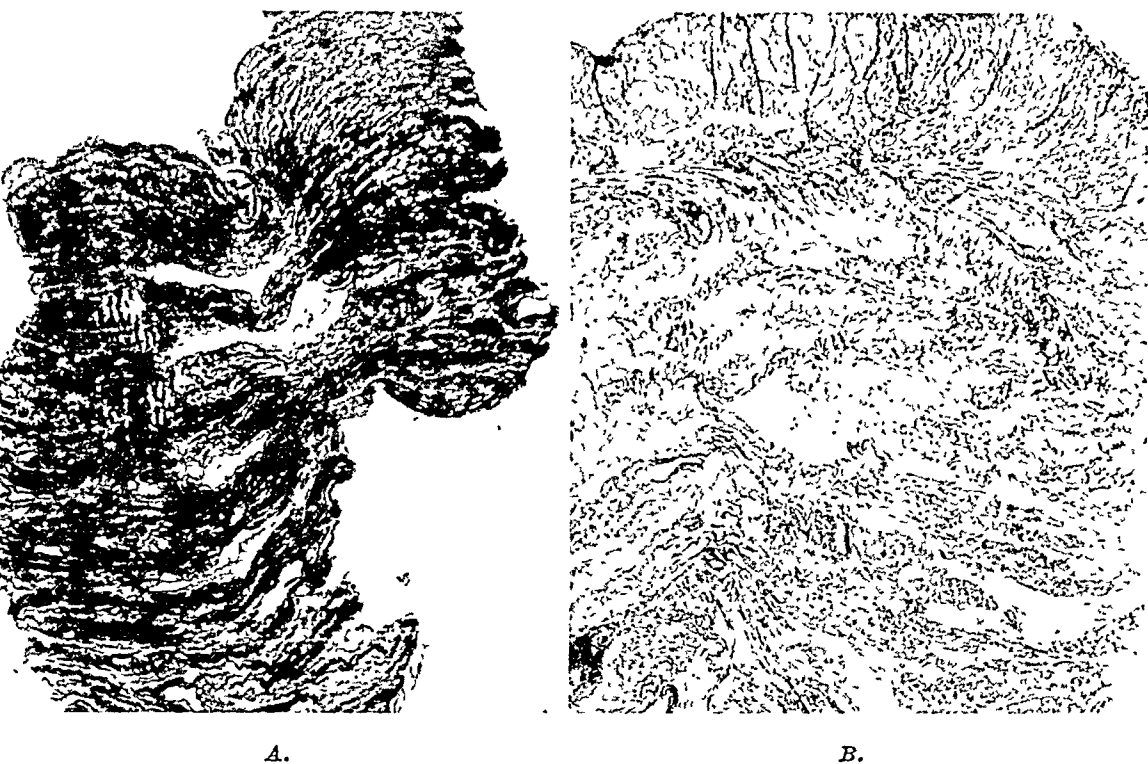
It is the opinion of the author that the former objections to spinal anesthesia do not hold if one (a) uses an initial dose not over 50 mg., (b) verifies stabilization of the blood pressure before emptying the uterus, and (c) uses only a 2.5 per cent anesthetic solution. These conditions are possible only when using the fractional method described by Lemmon.

One of the advantages of the classical operation is said to be a shorter operating time but this was not appreciable in our series. The supposed difficulty in incising and developing the bladder flap was not apparent since this procedure, in timed cases, was a matter of seconds. The shortest operation recorded was a Kerr cervical section which took exactly ten minutes. Labor is unnecessary to the performance of the low operation, since nearly half of our operations of this type were performed before labor began.

Adhesions due to a previous classical operation were found in thirty-eight instances compared to six where the previous operation had been of the low type. This incidence was twice as great as the relative proportion of operations. To prevent these adhesions Schumann advocates the development of a peritoneal flap before making a fundal incision but it would seem easier to use the peritoneal reflection already provided by nature.

Another factor not yet considered is the reported superiority of the low section in preventing subsequent rupture of the uterus. There

were three ruptured uteri following classical operations in this series, an incidence of 1 per cent. In addition, there were very thin scars in four more cases. One other rupture followed a Waters section but it occurred in the posterior wall of the fundus far removed from the scar. There were no ruptures of low scars. Elton⁷ reports an incidence of rupture of 1.5 per cent following thirty-three hundred classical operations. In contrast Waters,⁸ in a series of fifteen hundred sections, 70 per cent of which were of the low type, reports five ruptures following classical operations and none following the low. Grusetz and Tisdall⁹ were able to report only six cases of ruptured low transverse scars in the literature despite the increased performance of this operation. The opinion that the increased use of the low section will result in an equal incidence of ruptured scars is certainly unprejudiced by past performance.



Cesarean section morbidity and mortality

Fig. 1.—Photomicrograph (×20) of lower uterine segment A, and upper uterine segment B, stained for connective tissue (azocarmine). Note marked predominance of connective tissue in the lower uterine segment.

Comparable sections of the uterine wall (Fig. 1) taken from Kerr and fundal incisions when stained for connective tissue show a marked predominance of this tissue in the lower segment. In fact the lower uterine segment is covered by a real layer of fascia plainly visible at operation and well described as a continuation of the vesicovaginal fascia which thins out at Braun's ring. When closing the abdominal wall, it is upon fascia, not muscle, that one depends for strength and this likewise should apply to a uterine incision.

There were fifteen Porro operations performed, ten for uterine fibroids, three for ruptured uteri and two for uterine atony. The morbidity incidence was 13.3 per cent.

All five Waters operations were performed on patients who had been in labor over twenty-four hours, with an average duration of thirty-six hours. In every case the membranes had been ruptured prior to operation for an average of thirty hours. All the patients had one or more vaginal examinations before operation and there were preoperative temperature elevations in three instances. The morbidity incidence was 40 per cent with an average duration of three days.

If the proposition that septic death can rarely occur in an afebrile patient is valid, the morbidity figures at the Lying-in Hospital attest to the greater safety of the low operation for the patient in labor. The presence of postoperative adhesions is a decided disadvantage of the classical operation and may occasionally cause death from mechanical intestinal obstruction as reported by Manahan.¹⁰ There would seem to be little doubt that the low transverse incision offers increased protection against subsequent rupture of the scar. The morbidity rate for the Porro operation is low but all of these operations were performed in clean cases. On the other hand three of the Waters sections were definitely infected before operation, two of them having had prior intrauterine manipulations. The remaining two were cases of serious potential infection. The absence of signs of peritoneal irritation was remarkable considering the extent of infection preoperatively.

Since the deaths from postcesarean sepsis in any one hospital are not large, it was decided to study the records of such deaths provided through the courtesy of the Maternal Mortality Committee of the Philadelphia County Medical Society. From 1931 to 1942 inclusive, one hundred and fourteen deaths from sepsis followed cesarean section. Table V shows the distribution of these deaths by type of operation.

TABLE V. TYPE OF OPERATION AND DURATION OF LABOR IN FATAL CASES

| TYPE | NUMBER | HOURS OF LABOR | | | | | UNKNOWN |
|-----------------|--------|----------------|---------|----------|----------|---------|---------|
| | | 0 | 0 TO 12 | 12 TO 24 | 24 TO 48 | 48 PLUS | |
| Classical | 71 | 30 | 8 | 6 | 21 | 5 | 1 |
| Low | 20 | 2 | 2 | 4 | 9 | 1 | 2 |
| Porro | 8 | 3 | 1 | 1 | 2 | 1 | 0 |
| Extraperitoneal | 3 | 0 | 0 | 1 | 2 | 0 | 0 |
| Unrecorded | 12 | 4 | 3 | 2 | 2 | 1 | 0 |
| Total | 114 | 39 | 14 | 14 | 36 | 8 | 3 |

The twelve cases listed as "Unrecorded" were performed in 1931 and were undoubtedly classical in type. It will be noted that 70 per cent of the low and 100 per cent of the extraperitoneal compared to 45 per cent of the classical operations were preceded by a period of labor of twelve or more hours. In addition, the low operation was performed more often when other unfavorable conditions (Table VI) were present.

TABLE VI. ANTECEDENT FACTORS IN 114 SEPTIC DEATHS

| | |
|------------------------------------|-----|
| Operation after trial of labor | 65% |
| Duration of labor over 12 hours | 50% |
| Duration of labor over 24 hours | 38% |
| Ruptured membranes | 36% |
| Preoperative temperature elevation | 37% |
| Preoperative vaginal examination | 47% |

The distribution of cesarean sections in Philadelphia by type of operation in 1931 and 1941 has been reported by Lull.³ Comparison (Table VII) of the incidence of these operations with the distribution of deaths from sepsis according to type of operation for these two years shows an advantage in favor of the low operation.

This is less apparent in 1941 than 1931, probably as a result of the general trend toward increased use of the low section when unfavorable factors are present. More marked than this, however, is the very high death rate from the Porro operation which is usually thought of as the procedure of choice in the infected case. It will also be seen (Table VIII) that in 1941 all of the women dying from sepsis following the low or Porro operation had been in labor while death from sepsis following the classical procedure was preceded by labor in only half of the cases. Again it is seen that the Porro operation results in a high septic death rate.

TABLE VII. INCIDENCE OF OPERATIONS BY TYPE COMPARED TO PERCENTAGE OF DEATHS FROM SEPSIS IN 1931 AND 1941

| TYPE | 1931 | | 1941 | |
|-----------|-----------|--------|-----------|--------|
| | INCIDENCE | DEATHS | INCIDENCE | DEATHS |
| Classical | 79.9% | 85.0% | 61.5% | 60.0% |
| Low | 17.9% | 5.0% | 36.2% | 30.0% |
| Porro | 1.7% | 10.0% | 1.9% | 10.0% |

TABLE VIII. INCIDENCE OF DEATHS FROM SEPSIS BY TYPE OF OPERATION WITH PERCENTAGE IN LABOR IN 1931 AND 1941

| TYPE | 1931 | | | 1941 | | |
|-----------|--------|--------|----------|--------|--------|----------|
| | NUMBER | DEATHS | IN LABOR | NUMBER | DEATHS | IN LABOR |
| Classical | 458 | 3.4% | 70.5% | 550 | 1.1% | 50.0% |
| Low | 103 | 0.9% | 100.0% | 324 | 0.9% | 100.0% |
| Porro | 10 | 20.0% | 100.0% | 17 | 5.8% | 100.0% |

As the advantages of the Kerr section have become appreciated, it has been performed more frequently in potentially infected patients and the relative percentage of deaths from sepsis following its use has risen but the absolute percentage remains the same. Thus it would seem that this operation is safe for the patient who has been in labor twelve to twenty-four hours with no other unfavorable factors present. But what of the small group of neglected dystocia patients from which comes the majority of our septic deaths? Should we sacrifice the uterus or will an extraperitoneal operation offer as much or more protection? Reported series¹¹⁻²⁰ of Porro operations shows that most of these

are performed for fibroids, uterine atony, rupture or abruption and not for infection. Yet in Philadelphia the death rate from sepsis *alone* was 20 per cent in 1931, and 5.8 per cent in 1941 for all Porro operations. At the Lying-in Hospital only two Porro operations have been performed for infection during the past twelve years. One patient died of shock during the operation, the other died of peritonitis. Of the seventeen Porro operations performed in Philadelphia in 1941, only one was for infection and that patient died of peritonitis. Conversely, Waters* recently reported only two deaths from all causes in a total of two hundred and fifty extraperitoneal operations. Ninety of these were in patients septic before operation who had had more than forty-eight hours of labor. Positive cultures for pathogenic bacteria were obtained at operation in sixty instances. Irving¹¹ in 1937 compared the extraperitoneal with the Porro operations then recorded and showed that the latter had a 100 per cent higher mortality rate. If the remaining uterus is a focus of infection more important than peritoneal spill as a precursor to septic death, why do we fear death from peritonitis following uterine rupture where the focus is removed but peritoneal spill is not avoided. When one incises the lower uterine segment in an infected patient, that portion of the uterus most grossly contaminated is invaded and it would seem safer to confine the resultant spill to an extraperitoneal space which can be drained rather than to permit its entrance into the peritoneal cavity. At any rate, the fatal results from the

TABLE IX. MORTALITY FOLLOWING PORRO AND EXTRAPERITONEAL OPERATIONS

| PORRO | | | | | EXTRAPERITONEAL | | |
|------------------------------------|-------------|--------------|-------------------|----------------------------|---|--------|--------------|
| AUTHOR | TOTAL CASES | TOTAL DEATHS | NO. FOR INFECTION | NO. DEATHS IN SEPTIC CASES | AUTHOR | NUMBER | DEATHS |
| Greenhill ¹² | 38 | 0 | 1 | 0 | Steele ²¹ | 59 | 5 |
| Hawks ¹³ | 11 | 1 | 2 | 1 | Fleisher and Keeslmer ¹¹ | 19 | 0 |
| Lash and Cummings ¹⁴ | 53 | 6 | 12 | 4 | Hawks ¹³ | 30 | 0 |
| Adair ¹⁵ | 20 | 0 | 8 | 0 | Burns ²¹ | 79 | 2 |
| Phaneuf ¹⁶ | 25 | 0 | 7 | 0 | Cosgrove ²¹ | 74 | 2 |
| Lazard ¹⁷ | 39 | 0 | 1 | 0 | Irving ¹¹ | 23 | 0 |
| Daily ²⁵ | 30 | 0 | 30 | 0 | Sackett ¹¹ | 51 | 4 |
| Maxwell ¹⁸ | 11 | 2 | 2 | 1 | Perrins ¹¹ | 22 | 0 |
| Lazard ¹⁹ | 51 | 4 | 9 | 2 | Holterman ¹¹ | 194 | 10 |
| Arnot ²⁰ | 10 | 2 | 10 | 2 | Waters | 90 | 2 |
| Briscoe | 27 | 5 | 3 | 3 | Eisaman and Austin ²² | 22 | 0 |
| | | | | | Williamson and Goldblatt ²³ | 25 | 0 |
| | | | | | Pieri and Irving ²⁴ | 20 | 0 |
| | | | | | Briscoe | 9 | 0 |
| Total | 315 | 20 (6.3%) | 85 | 13 (15.2%) | | 717 | 25 (3.4%) |

*Reported at a meeting of the Obstetrical Society of Philadelphia, February 3, 1944.

Porro operations performed for infection in this city compared to the results of our own and reported series²¹⁻²⁵ of extraperitoneal operations would prove this to be more than mere speculation.

Summary

1. Cesarean section performed before labor begins offers the patient the most protection against sepsis.

2. Postcesarean morbidity rates at the Philadelphia Lying-in Hospital during the past three years show superiority of the low section over the classical for the elective case and especially for the patient in labor.

3. Over a third of the women who die in Philadelphia following cesarean section die of sepsis.

4. One-half of these deaths occurred in patients who had been in labor over twelve hours before operation, 37 per cent of whom showed signs of sepsis preoperatively.

5. The absolute death rate and the relative death rate from sepsis show superiority of the low operation for the elective case and especially for the patient in labor.

6. The supposed protection of the Porro operation for the infected patient has been lacking in Philadelphia during the past twelve years.

7. Reported series of extraperitoneal operations shows the death rate from all causes to be from two to five times less than the death rate from sepsis alone for the Porro operations performed in this city.

8. The operation of choice for the infected patient would seem to be an extraperitoneal cesarean section.

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255 SOUTH SEVENTEENTH STREET

Discussion

DR. CLIFFORD B. LULL.—Surveys of cesarean sections which we made in 1931, and again in 1941, showed that the mortality rate depends on three factors: first, the time the operation was done; second, the type of operation performed; and third, the anesthesia that was used. Dr. Briscoe's paper brought out all of these three factors again. I still believe that there is a place in obstetrics for the low classical cesarean section. For example, the patient who has had a previous cesarean operation and is going to be sterilized at operation performed at the time of election, is a suitable case for the low classical. In doing the low segment operation, I believe that the Kerr incision is better than the longitudinal, but in certain cases where the head is unusually large, we do the longitudinal incision because it may be extended, allowing us to deliver the head more easily. As to the Porro operation, Dr. Briscoe brought out a very interesting point; namely, that women potentially infected are just as likely to die following this as after one of the other types of section, except the extraperitoneal. We have not had an opportunity to do very many of the Waters' type of section. Those that we have seen, however, were all potentially infected women who had been in labor a long time, but who made a very satisfactory convalescence. I believe it will be some time before any of us will have an opportunity of doing very many of this type as most of our cases are sectioned before they reach the point of potential infection.

DR. JOHN COOKE HIRST, II.—The topic is timely because we are still discussing the relative advantages of classical vs. low operations, and Dr. Waters has demonstrated that we did not know all there is to know about cesarean section. Also, Dr. James S. Taylor, Chairman of the Pennsylvania State Maternal Welfare Commission has been greatly concerned about poor results from cesarean sections for many years. I have a report of the first six months of 1941, where we see a total of 86,000 births and 209 maternal deaths in Pennsylvania, of which the largest cause of deaths was eclampsia with 38 cases, but 28 cesarean deaths, not counting 11 additional deaths where cesarean section was done for other reasons, which might be attributed to the operation, so that we certainly can improve our cesarean section results according to this analysis.

I am particularly interested in the subject because of experience with a type of transperitoneal exclusion low cesarean section for the frankly infected case rather than hysterectomy, namely the Pfannenstiel-Kerr-B. C. Hirst procedure, which was not done by my late father, but utilizes his exclusion principle with good results. You are familiar with a similar technique described by Dr. Erwin Smith of New York, and Dr. Frost of Morristown, N. J. There is no question that sulfonamide has imposed an obligation on us that is, rather than rely on hysterectomy, to become thoroughly comfortable in doing some type of exclusion or extraperitoneal operation, of which I think the Waters is the best. My own personal preference is, first, the Kerr operation for the elective case, then the Beck section for the doubtful patients, and the transperitoneal operation for the obviously infected patient—all of them to be done under continuous caudal or spinal anesthesia.

DR. OWEN JONES TOLAND.—There is a question that I should like to ask Dr. Briscoe, whether or not the cases that he refers to as dying of peritonitis were actually proved by autopsy to be peritonitis. In my own experience, I have found death following cesarean section to be most unusually associated with peritonitis;

the cause of death has been sepsis, yes, but the septic process has extended via the uterine wall, through lymphatics, to the parametrial tissue and to the blood stream. The peritoneal cavity has not been invaded. It is true that many of these cases have a paralytic ileus, and I have often wondered if many of the cases described in the Report of the Mortality Committee as dying of peritonitis, are not actually sepsis with paralytic ileus and without peritonitis.

DR. BRISCOE (closing).—The Kerr operation was stressed by me, first, because our morbidity statistics were compiled chiefly from this procedure. Second, it is a simple geometric fact that a curved incision affords more room for extracting the fetus. Last, the protection against subsequent rupture applies more correctly to this operation. Kletzhändler (AM. J. OBST. & GYN. 47: 132, 1944) reviewed the reports of 402 cases of rupture of the uterus; 196 followed fundal incisions, 87 longitudinal cervical incisions, but only 5 occurred after transverse cervical incisions. There was no information in the remaining 104 cases. The lower uterine segment is predominately connective tissue, and it is possible to place a low-curved transverse incision entirely within this area which will be strong, whereas the cervical longitudinal incision almost invariably extends up into the weaker, muscular portion of the fundus.

Sulfanilamide powder should certainly be used as suggested by Dr. Hirst. This does not always overcome the infectivity of the peritoneal spill, however, for in the first nine months of 1943, five of the seven women who died of sepsis had generalized peritonitis despite the use of this drug.

To answer Dr. Toland's question, let me state that 80 per cent of the 45 patients who were autopsied had peritonitis. It was present following the different procedures in these percentages: classical 80 per cent, Porro 100 per cent, low cervical 66.6 per cent and extraperitoneal 50 per cent.

I have an additional table showing the results of reported series of Porro and extraperitoneal operations mentioned in the paper. The mortality incidence for 315 Porro operations was 6.3 per cent. However, only 85 of these were done for actual or potential infection with a death incidence in this group of 15.2 per cent. Compared to this are 717 extraperitoneal operations with a mortality incidence of only 3.4 per cent.

Dr. Williams is correct in stating that we should have a "maternal protection society" since 4 per cent of our cesarean sections (in this city), are done in the presence of neglected dystocia. What this really means is that 40 women every year need the added protection of an extraperitoneal operation. This should remove any doubts from the minds of those who state that here in Philadelphia, there is no need for the Waters' operation at this time of enlightened practice.

ZONDEK'S SIMPLIFIED TREATMENT OF SECONDARY AMENORRHEA

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CESSTION of cyclic uterine bleeding in the nonpregnant woman of childbearing age with intact pelvic organs is sometimes a source of grave concern to the patient and her family; frequently women thus afflicted develop various neuroses and depressive states. Therefore, it is often imperative to produce uterine bleeding in order to reassure the patient and help her toward an adjustment of her problems; in many instances this should be done in the shortest possible time. Whether the uterine bleeding induced is a physiological menstruation or the result of substitution therapy is immaterial to the patient; the external manifestation of uterine bleeding suffices to reassure her that the normal function was not completely lost.

In a large number of cases amenorrhea is due to pelvic pathology, debilitating diseases, nutritional deficiencies and psychogenic disturbances. Hereditary tendencies, too, must be considered, as well as diseases and tumors of the central nervous system and of the endocrine glands. In the balance of the cases the disorder is endocrine in origin. As a matter of fact, the various types of functional amenorrhea constitute the majority of amenorrheic cases. The glands which are commonly concerned are the thyroid, the pituitary, the ovaries, and the adrenals.

Amenorrhea caused by thyroid disturbances is comparatively rare; when encountered it readily responds to treatment. Amenorrhea due to a mild pituitary or ovarian deficiency often responds to stimulative glandular therapy. However, the more severe types of amenorrhea, which are due either to adrenal overactivity or to the primary pituitary or primary ovarian deficiency rarely respond to stimulative therapy; in these instances substitution therapy with potent estrogens and progestogens is indicated.

Ever since glandular and hormonal preparations became available, the medical profession has sought earnestly for a treatment plan which is both simple and effective in inducing uterine bleeding. The commercial production of estradiol and its derivatives as well as of progesterone paved the way for further progress in this direction. Considerable advance in simplifying the heretofore commonly employed cyclic hormonal therapy of secondary amenorrhea was made by Zondek¹ who demonstrated that out of a group of 17 patients with secondary amenorrhea of from 6 months to 9 years' duration, 11 cases (64.7 per cent responded favorably to the simultaneous administration of progesterone, 12.5 mg., and of estradiol benzoate, 2.5 mg. each on two consecutive

days. Bleeding ensued 48 to 112 hours after the second injection and the majority of nonreactors were found to be those patients who had been amenorrheic for more than 2 years. Therefore in order to improve the percentage of positive results Zondek suggests that the two-day treatment plan should be restricted to cases of less than 2 years' duration.

Berlind² presenting 9 cases of secondary amenorrhea, employed Zondek's simplified technique in 7 patients, 3 of whom had been amenorrheic for more than two years. In these latter cases, though, bleedings induced by other hormonal measures had preceded the two-day treatment and thus the responsiveness to the condensed therapy was probably greater than was to be expected in view of the duration of the amenorrhea. For all practical purposes therefore, all of Berlind's 7 patients subjected to the two-day treatment plan, they received a total of 9 courses, may be considered as falling into the group of amenorrhea of less than 2 years' duration. In each single instance, bleeding occurred, 2 to 4 days after the second injection.

Method

The simplicity of the new method of treatment suggested its application in our series of 31 patients with secondary amenorrhea ranging in age from 15½ to 38 years with an average age of 23. As is seen in Table I, the duration of amenorrhea was from 2 months to 7 years. The disorder in all patients was due to pituitary or ovarian failure.

Treatment consisted of the administration of estradiol benzoate, 2.5 mg., and progesterone, 12.5 mg., which were drawn into one syringe and injected intragluteally; the same procedure was followed the ensuing day. In the chart application of this plan is shown in the columns "Therapy" and "Follow-up" respectively by merely indicating the days on which the injections were administered. Combined estrogenic-progestogenic therapy, differing in the plan of administration from the two-day treatment plan, is designated in the table as such. Estrogenic therapy alone, or progestogenic therapy alone, or stimulation therapy is similarly indicated in the table.

Results

Uterine bleeding resulted in 25 patients (80.6 per cent). In some instances (Cases 4, 5, 6, 10, 12) two courses of therapy were given and one patient (Case 8) received three series of two injections each. The total number of courses of treatment, 38, elicited 31 positive responses (81.5 per cent). In general, bleeding ensued 4 to 6 days following the second injection but there were also shorter as well as longer intervals. The amenorrhea in two of the 6 patients who failed to respond (Cases 1, 12, 18, 23, 27, 28) was of more than two years' duration. Four of these showed marked hypoplasia of the uterus. In four patients (Cases 17, 19, 20, 24), the first bleeding episode produced by the two-day treatment was followed by menstruation occurring spontaneously at four-

TABLE I. CLINICAL FEATURES OF 31 CASES OF SECONDARY AMENORRHEA AND RESULTS OF TREATMENT WITH THE TWO-DAY ZONDEK PLAN

| NO. | PATIENT'S INITIALS | AGE | HT. WT. IN. LB. | BODY BUILD | MENSTRUAL AND OBSTETRICAL HISTORY | DURATION OF AMENORRHEA. | PELVIC (P.) OR RECTAL (R.) EXAMINATION | LABORATORY INVESTIGATIONS | THERAPY | BLEEDING EPISODE | FOLLOW-UP |
|-----|--------------------|-----|-----------------|---------------------------|---|-------------------------|---|--|----------------------|------------------|---|
| 1 | Mrs. L. F. | 38 | 61½ 145 | N. to S. | 12x28x4 | 7 yr. | P.: Neg. | B.M.R. -10% End. biopsy: Resting phase B.M.R. +20% | 9 / 2- 3/42 | None | Did not report |
| 2 | Miss A. L. | 27 | 62 130 | N. to S. | 15x28x7 | 4 yr. | R.: Neg. | B.M.R. -8% | 9/22-23/42 | 10/ 2/42 | Did not report |
| 3 | Miss M. G. | 18 | 64½ 124 | N. to S. | 16x6 mo.-1 yr. x1 | 11 mo. | R.: Neg. | B.M.R. -17% | 10/19-20/42 | 10/21/42 | Did not report |
| 4 | Miss J. R. | 16 | 63½ 130 | N. to S. | 13x6 mo. x5 | 10 mo. | P.: Neg. | B.M.R. -5% | 11/18-19/42 | 11/26/42 | 12/22-23/42: bleeding 12/27/42 |
| 5 | Miss A. K. | 17 | 66½ 148 | N. to S. | 12x6 wk.-6 mo. x4 | 6 mo. | R.: Neg. | B.M.R. -2% | 12/31/42- 1/ 1/43 | 1/ 7/43 | 2/13-14/43: bleeding 2/21/43 |
| 6 | Miss T. S. | 18½ | 62 125 | N. to S. | 12x6 mo.-1 yr. x3 | 7 mo. | R.: Neg. | B.M.R. -2% | 1/24-25/43 | 1/31/43 | 2/22-23/43: bleeding 2/28/43. Stimulation therapy: no response |
| 7 | Miss A. B. | 16 | 60½ 90 | N. to S. | 12x28x7 | 3 mo. | P.: Neg. | B.M.R. -2% | 2/ 2- 3/43 | 2/ 7/43 | Did not report |
| 8 | Miss E. S. | 17 | 60½ 107 | N. to S. | 12x4-6 wk x5-7 | 10 mo. | R.: Neg. | B.M.R. -2% | 3/22-23/43 | 3/30/43 | 4/24-25/43: bleeding 4/29/43 |
| 9 | Mrs. B. W. | 35 | 61 150 | Obese | 11x1-4 mo. x3 1 child, 8 yr. old | 16 mo. | P.: Neg. | | 5/ 8- 9/43 | 5/15/43 | 9/21-22/43: bleeding 9/29/43 Estrogenic therapy: bleed- ing 6/12/43. Spon- taneous bleeding 8/6/43. |
| 10 | Mrs. L. S. | 30 | 60½ 150 | Obese | 18x1-4 mo. x3 2 children aged 8 yr. & 8 mo. respectively | 9 mo. | P.: Para- metritis | B.M.R. -10% | 5/15-16/43 | 5/22/43 | 11/6-7/43: bleeding 11/15/43 8/28-29/43: bleeding 9/4/43 |
| 11 | Mrs. P. C. | 24 | 67½ 168 | Obese, male escent. | 11x28-5 mo. x3 | 6 mo. | Hypoplastic uterus; en- larged ovaries | B.M.R. -1% End. biopsy: Early prolif- erative phase | 6/ 3- 4/43 | 6/ 9/43 | Stimulation therapy: bleeding 8/18/43 |

| | | | | | | | | | | | | |
|----|------------|----|-----|-----|-----------------------------|---|--------|--|--|------------|---------|---|
| 12 | Mrs. A. T. | 24 | 62 | 128 | N. to S. | 14x28x31 Stillborn child 7 mo. previous | 7 mo. | P.: Hypo- plastic uterus | B.M.R. +4% | 6/ 8- 9/43 | None | Combined estrogenic pro- gestogenic therapy: no response 7/10-11/43: no response Estrogenic therapy: bleeding 7/20/43 Spontaneous bleeding 9/27/43 Did not report |
| 13 | Mrs. M. M. | 30 | 63½ | 170 | Obese, male escut. | 13x1 mo.-1 yr. x5 | 5 mo. | P.: Neg. | B.M.R. -15% | 6/ 8- 9/43 | 6/15/43 | Estrogenic therapy: bleeding 7/20/43 Spontaneous bleeding 9/27/43 Did not report |
| 14 | Miss L. S. | 16 | 63 | 126 | N. to S. | 10x30x5 | 7 mo. | R.: Ovarian cyst | B.M.R. -10% | 6/ 9-10/43 | 6/16/43 | Did not report |
| 15 | Miss G. B. | 28 | 63½ | 123 | N. to S. | 16x3-6 mo. x3- 4 | 5 mo. | R.: Neg. | B.M.R. +18% | 6/10-11/43 | 6/18/43 | Estrogenic therapy: bleeding 7/6/43 Stimulation therapy: bleeding 9/14/43 Stimulation therapy: no response |
| 16 | Miss H. G. | 17 | 63 | 137 | Male escut. | 16x4 mo. x2 3 induced bleedings | 2 mo. | R.: Neg. | B.M.R. +8% | 6/13-14/43 | 6/22/43 | Stimulation therapy: no response |
| 17 | Miss C. G. | 18 | 60½ | 130 | N. to S. | 13x1-3 mo. x3 | 3 mo. | R.: Neg. | B.M.R. -9% | 6/22-23/43 | 6/28/43 | Spontaneous bleedings: 7/26/43, 8/23/43, 9/20/43, 10/18/43, 11/16/43, and 12/30/43 Did not report |
| 18 | Mrs. R. G. | 25 | 61½ | 199 | Obese | 11x28x3 | 5 yr. | P.: Hypo- plastic uterus | B.M.R. +12% | 6/25-26/43 | None | Did not report |
| 19 | Miss H. K. | 20 | 63½ | 106 | N. to S. hypo- mastia | 15x6 wk.-6 mo. x7 | 2 mo. | P.: En- larged right ovary | B.M.R. -9% | 6/28-29/43 | 7/16/43 | Spontaneous bleedings: 8/28/43 |
| 20 | Mrs. G. G. | 23 | 61½ | 123 | N. to S. | 11½x1-3 mo. x3-5 | 5 mo. | P.: Neg. | B.M.R. +3% End. biopsy: Proliferative phase | 7/14-15/43 | 7/22/43 | Spontaneous bleeding 9/7/43 |
| 21 | Miss A. L. | 25 | 64 | 142 | N. to S. | 12x1-6 mo. x4 | 4 mo. | P.: Para- metritis | | 8/16-17/43 | 8/22/43 | Stimulation therapy: bleeding 9/27/43 Did not report |
| 22 | Miss M. G. | 19 | 62 | 104 | N. to S. Male escut. | 17x2-8 mo. x2 | 7 mo. | P.: Neg. | | 8/17-18/43 | 8/23/43 | Did not report |
| 23 | Mrs. L. P. | 35 | 62 | 136 | N. to S. | 15x28-2 mo. x3 | 17 mo. | P.: Hypo- plastic pel- vic viscera | | 8/25-26/43 | None | Stimulation therapy: no response |

TABLE I—CONT'D

| NO. | PATIENT'S INITIALS | AGE | HT. IN. | WT. LB. | BODY BUILD | MENSTRUAL AND OBSTETRICAL HISTORY | DURATION OF AMENORRHEA | PELVIC (P.) OR RECTAL (R.) EXAMINATION | LABORATORY INVESTIGATIONS | THERAPY | BLEEDING EPISODE | FOLLOW-UP |
|-----|--------------------|-----|---------|---------|----------------------|--|------------------------|--|---------------------------|-------------|------------------|---|
| 24 | Miss B. O. | 16 | 58 | 118 | N. to S. | 13x5-6 wk. x4 | 2½ mo. | P.: Neg. | B.M.R. -20% | 9/ 7- 8/43 | 9/15/43 | Spontaneous bleedings 10/12/43, 11/11/43, and 12/20/43 Did not report |
| 25 | Miss D. S. | 20 | 64½ | 110 | N. to S. Male esent. | 13x28x3 to age of 17; from there on irregular and longer intervals | 8 mo. | R.: Neg. | B.M.R. +19% | 9/15-16/43 | 9/21/43 | |
| 26 | Mrs. H. B. | 27 | 65 | 145 | N. to S. | 14x2-3 mo. x3 1 child aged 11 mo. | 6 mo. | P.: Neg. | B.M.R. -10% | 9/15-16/43 | 9/23/43 | Did not report |
| 27 | Miss A. G. | 29 | 65 | 120 | N. to S. | 16x6-8 mo. x2-3 | 17 mo. | P.: Hypo-plastic uterus R.: Neg. | B.M.R. -29% | 9/22-23/43 | None | Progestogenic therapy: no response |
| 28 | Miss J. S. | 15½ | 66 | 142 | Hypo-mastia | 14x1-7 mo. x2 | 6 mo. | R.: Neg. | B.M.R. -18% | 9/23-24/43 | None | Did not report |
| 29 | Mrs. M. S. | 24 | 63½ | 123 | N. to S. | 16x28x2-3 1 miscarriage 3 yr. ago | 3 mo. | P.: Oophoritis and parametritis | B.M.R. -10% | 10/ 3- 4/43 | 10/10/43 | Did not report |
| 30 | Mrs. C. D. | 23 | 68 | 183 | Obese | 16x3-8 mo. x8-14 | 4 mo. | P.: Small uterus; right ovarian tenderness | B.M.R. -13% | 10/16-17/43 | 10/20/43 | Did not report |
| 31 | Miss G. S. | 20 | 63½ | 132½ | Normal | 13x6 wk.-5 mo. x3 | 3 mo. | R.: Neg. | B.M.R. +13% | 10/25-26/43 | 11/ 2/43 | |

week intervals. Two of these patients (Cases 19, 20) reported one such bleeding; one girl (Case 24) menstruated three times and one (Case 17) had six spontaneous consecutive periods. There were spontaneous bleeding episodes also in other patients of the series but these had received other therapeutic measures intermittently and therefore their spontaneous responses are not detailed here. While it is not to be expected that hormonal therapy of but two days' duration—regardless of its efficacy in producing bleeding—would alter the pattern of the endometrial mucosa, it was desirable to study pre- and postmedication endometrial biopsy specimens in some patients.

The following history of a patient exemplifies both procedure and observations in this series.

Case Report

Mrs. P. C., white, aged 23, married 2½ years, was first seen on April 27, 1942. Her chief complaints were sterility and protracted periods of amenorrhea for the past eight years.

Past History: Menarche was at the age of 11. Periods were regular for 4 years, occurring every 28 days and lasting from 4 to 5 days. Since the age of 15, however, menstruation occurred only every 4 to 6 months. Coincidental with this oligomenorrhea she noticed a gradually increasing hypertrichosis of the face, chest and abdomen, decreased vitality and frequent attacks of abdominal pain. The patient had had mastoiditis and pyelitis at the age of 10; no other serious illness or operation was reported. A congenital defect of both eyes (conical cornea) had been noted by an ophthalmologist several years previously and this was confirmed by Dr. Andrew Rados on May 8, 1942. During the past 4 years, the patient had medical attention for amenorrhea and sterility and received intensive hormonal therapy to which she responded occasionally by staining. The last episode of staining in November, 1941, was brought on by intensive estrogenic therapy.

Physical Examination: Height 67½ inches, weight 168 pounds; patient exhibited some traits of masculinity such as hirsuties of the face, chest and extremities. The blood pressure was 130/70 mg. Hg and the pulse rate 56. The urinalysis was negative for albumin and sugar. A study of the blood chemistry revealed the following findings: sugar, 113 mg. per cent; cholesterol, 180 mg. per cent; and uric acid, 1.5 mg. per cent. The basal metabolic rate was normal (minus 1 per cent). Pelvic examination revealed an enlarged clitoris (2½ cm.), a narrow vaginal orifice and a hypoplastic uterus. The cervix was elongated so that the cervix-body ratio was 2:1. Both ovaries were enlarged and apparently cystic.

The patient was subjected to estrogenic therapy which elicited bleeding in June, 1942. In view of the presence of signs of masculinization (hypertrophy of the clitoris, hirsutism), it was decided to perform an exploratory laparotomy with the object of determining the presence or absence of testicular tissue or any masculinizing tumor. The operation performed on July 15, 1942, by Dr. Charles Robbins, disclosed enlarged sclerotic ovaries and a chronically inflamed appendix. The adrenal glands were palpated but no enlargement could be detected. A wedge-shaped excision of the midportion of both ovaries and an appendectomy were carried out. The patient's recovery was uneventful. Histologic examination of the resected ovarian tissue revealed several



Fig. 1.—Case 11, premedication endometrial biopsy showing proliferative phase.

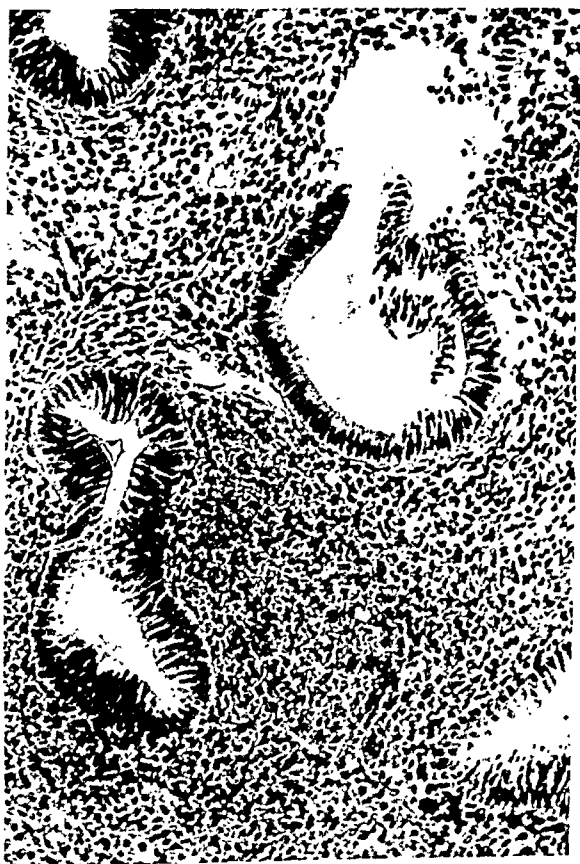


Fig. 2.—Case 11, postmedication endometrial biopsy showing proliferative phase.

immature follicular cysts and corpora albicantia; there was also evidence of increased fibrosis.

Since resumption of menstruation did not occur following the operation, the patient received both stimulative and substitutive hormonal therapy for a period of 6 months. Bleeding episodes resulted, however, from substitution therapy only. The last period elicited by estrogen-progesterone therapy having occurred on March 31, 1943, it was decided to subject the patient to the simplified two-day treatment. This was also advisable since she moved out of town and was unable to make frequent visits to the office. On June 3, more than 2 months after the last injection of any hormonal preparation, a premedication endometrial biopsy was taken. The histologic picture of the specimen was typical of an early proliferative phase (Fig. 1). Immediately after obtaining the biopsy specimen, estradiol benzoate, 2.5 mg., and progesterone, 12.5 mg., were administered, and the same dose was repeated the following day. The postmedication biopsy specimen taken on June 5, revealed no change as compared with the biopsy specimen of two days previously—the pattern was again that characteristic of the proliferative phase (Fig. 2). Therapy resulted in uterine bleeding on June 9. No further spontaneous periods occurred.

Discussion

When Zondek, Rozin and Vesell³ demonstrated that there was no need for inducing complete proliferation of the endometrium with estrogens in order to elicit uterine bleeding with progesterone, the groundwork was laid for further simplification of effective treatment of secondary amenorrhea. The obvious advantage of the 2-day treatment plan subsequently devised by Zondek as compared with the heretofore commonly employed method of treatment devised by Kaufmann⁴ can be clearly demonstrated by comparing a table, as given by Kaufmann (Table II), portraying a general outline for a treatment plan of amenorrhea and a table (Table III) depicting similarly the two-day Zondek technique. As can be easily seen, Kaufmann advocates no less than 10 injections, 5 consisting of estradiol benzoate, 5 mg. each, and an equal number of progesterone, 5 mg. each, spaced over a period of more than 3 weeks, with the expectation that menstruation will be produced on the twenty-fifth day after initiation of treatment. The Zondek plan, on the other hand, calls for 2 injections only to be given on consecutive days with a total requirement of 5 mg. estradiol benzoate and 25 mg. progesterone. While the amounts of progesterone needed are identical for both techniques, the Zondek plan obviates the use of large doses of estrogen, i.e., only 5 mg. of estradiol benzoate as contrasted with 25 mg. administered according to Kaufmann's recommendations. Moreover, the fact that large doses of estrogen may have an inhibitory effect on the anterior pituitary must be considered. Finally, shortening of the duration of therapy from 25 days to 6 days (2 days for actual treatment and averagely 4 days before onset of bleeding) is of great value in many instances.

TABLE II

| SUNDAY | MONDAY | TUESDAY | WEDNESDAY | THURSDAY | FRIDAY | SATURDAY |
|--------|---------------------------|---------|-----------|---------------------|--------|--------------|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| 7 | 8 | 9 | 10 | 11 | 12 | 13 |
| 14 | 15 | 16 | 17 | 18 | 19 | 20 |
| 21 | 22 | 23 | 24 | 25 | 26 | 27 |
| | Estradiol benzoate, 5 mg. | | | Progesterone, 5 mg. | | Menstruation |

TABLE III

| SUNDAY | MONDAY | TUESDAY | WEDNESDAY | THURSDAY | FRIDAY | SATURDAY |
|--------|--|---------|-----------|----------|--------|----------|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| 7 | 8 | 9 | 10 | 11 | 12 | 13 |
| 14 | 15 | 16 | 17 | 18 | 19 | 20 |
| 21 | 22 | 23 | 24 | 25 | 26 | 27 |
| | Estradiol benzoate, 2.5 mg. + progesterone, 12.5 mg. | | | | | |
| | Uterine bleeding | | | | | |

Table portraying Zondek's two-day treatment plan of amenorrhea.

Zondek suggested that the 2-day treatment plan be restricted to cases of less than 2 years' duration. That such limitations should be considered is borne out by the fact that in two of our nonreactors, the amenorrhea was of more than 2 years' duration. On the other hand, in Case 2 of the series presented the amenorrhea was of 4 years' standing—nevertheless, the patient responded promptly to the two-day treatment plan. The comparative results recorded by Zondek, by Berlind, and by us are shown in Table IV.

TABLE IV. COMPARATIVE RESULTS WITH ZONDEK'S TWO-DAY TREATMENT PLAN

| | NO. OF CASES | NO. OF POSITIVE RESULTS | PER CENT |
|----------------|--------------|-------------------------|----------|
| Zondek | 17 | 11 | 64.7 |
| Berlind | 7 | 7 | 100.0 |
| Present series | 31 | 25 | 80.6 |

Summary and Conclusions

A series of 31 patients with secondary amenorrhea due to pituitary or ovarian deficiency is presented and the results with the simplified two-day treatment plan described. This method devised by Zondek consists of the injection of a combination of estradiol benzoate, 2.5 mg., and progesterone, 12.5 mg., on two consecutive days. Uterine bleeding was produced in 25 patients (80.6 per cent). Among the 6 nonreactors were 4 patients with marked uterine hypoplasia. In two of the unresponsive patients, the amenorrhea had persisted for more than 2 years. By restricting the simplified treatment plan to patients with an amenorrhea of less than 2 years' duration, the percentage of favorable responses (80.6 per cent in our series) can probably be further increased. No marked changes were produced in the endometrial pattern with the 2-day treatment as evidenced by the pre- and postmedication biopsy specimens which are presented.

The advantages of the simplified method are discussed. The 2-day treatment plan should be employed in all those instances of functional amenorrhea of less than 2 years' duration where thyroid medication has failed to yield results and where for some reason or another, it is desirable or imperative to obtain uterine bleeding in as short a period of time as possible.

Acknowledgment: The special combination packages for the simplified two-day treatment of amenorrhea consisting of 2 ampoules of Dimenformon Benzoate (each representing 2.5 mg. of estradiol benzoate) and 2 ampoules of Progestin (each representing 12.5 mg. of progesterone), employed in this study, were liberally supplied by Roche-Organon, Inc., Nutley, New Jersey, through the courtesy of Dr. Leo Pirk.

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CORD TRANSFUSIONS IN NEWBORN INFANTS*

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(From the Department of Obstetrics of the Methodist Hospital)

GREAT emphasis has been placed on the prevention of maternal mortality, with considerable success. Today it seems fitting to turn our attention to the mortality among infants, where a proportionate success is still to be achieved.

The greatest loss of life among infants is during the first twenty-four hours, and Holt and McIntosh¹ state that "if the infant survives for the first forty-eight hours after birth its chances are immeasurably improved; various clinics have reported [mortality] rates of 3 to 9 per cent if these early deaths are excluded."

The responsibility for the first twenty-four hours is the obstetrician's; deaths in that period come under the obstetric, not the pediatric, service. Thus the question arises, what can be done by the obstetrician to increase the chances of newborn infants to survive the first forty-eight hours? The usual treatment suffices if the babies are full term and if they are not suffering from the effects of a long labor or some blood dyscrasia. But for prematures, infants affected by difficult labor and those with hemorrhagic disease or erythroblastosis, special treatment must be instituted, and the sooner the better.

This paper presents a method of transfusion with citrated adult blood given immediately after birth through the umbilical vein. The procedure is prophylactic in cases of prematurity, difficult labor and a history in the mother of previous stillbirths, prematures and early deaths.

In 1937, Wilson² reported the use of lobelin by way of the umbilical vein in cases of difficulty in spontaneous respiration and described in detail the method of administration. After using lobelin in this way in several cases, it occurred to the writer that adult blood might be given by the same route, particularly for prematurity. Such a transfusion was first given at the Methodist Hospital in Brooklyn in 1940, and the case was reported before the New York Obstetrical Society the same year. The infant, which survived, weighed 4 pounds, 4 ounces and was of 28 weeks' gestation; the mother had lost two previous premature infants (see Case Report 1, Mrs. D. A.). In the next two years 5 more cord transfusions were done in prematures, and in 1943, 12, a total of 18 cord transfusions in prematures in a four-year period. In addition

*This study aided by a grant from the Lindridge Research Fund.

in 1943, the method was used in 16 full-term infants, making a total of 34 cord transfusions in newborn infants from 1940 through 1943.

Three tables follow. Table I gives maternal and fetal mortality statistics at the Methodist Hospital in Brooklyn for the four years, 1940 through 1943. Table II is a summary of the 18 transfusions in prematures, and Table III of the total 34 transfusions.

TABLE I. MATERNAL AND INFANT MORTALITY STATISTICS
METHODIST HOSPITAL 1940-1943

| YEAR | LIVING INFANTS* | | | | | INFANT DEATHS | | | |
|-------|------------------|-----------------|-------------|------------|-----------|---------------|-----------|-----------|---------|
| | TOTAL DELIVERIES | MATERNAL DEATHS | STILLBIRTHS | FULL TERM | PREMATURE | TOTAL | FULL TERM | PREMATURE | TOTAL |
| 1940 | 1,726 | 2 | 68 | 1,601 | 72 (1) | 1,673 (1) | 9 | 23 | 32 |
| 1941 | 1,865 | 2 | 77 | 1,722 | 88 (3) | 1,810 (3) | 13 | 18 (1) | 31 (1) |
| 1942 | 2,086 | 3 | 84 | 1,922 | 100 (2) | 2,022 (2) | 16 | 20 | 36 |
| 1943 | 2,167 | 2 | 94 | 1,999 (16) | 94 (12) | 2,093 (28) | 7 (1) | 20 (2) | 27 (3) |
| Total | 7,844 | 9 | 323 | 7,244 (16) | 354 (18) | 7,598 (34) | 45 (1) | 81 (3) | 126 (4) |

*Many of the premature infants were nonviable, but if they breathed following delivery they were included in this table.

() Numbers in parentheses indicate infants given cord transfusions.

Results

The 18 infants classified as prematures weighed under 5½ pounds, and gestation with one exception was from 23 to 36 weeks. The exception was a twin weighing 4 pounds, 14 ounces, gestation 39 weeks. There were 3 deaths among the prematures, a mortality of 16.6 per cent. Mother's blood was used in 16 with 2 deaths, one in a nonviable infant; father's blood was used in 1; professional donor's blood was used in 1, with death of the infant.

Four of the prematures weighed less than three pounds and the only one to die weighed 1 pound, 6 ounces. Five weighed from three to four pounds, and the only one lost followed a breech delivery. Weight of the infant was 3 pounds, 11 ounces; 30 c.c. of mother's blood were given. The infant lived 15 hours; blood was aspirated from the throat. Nine weighed from four to five and a half pounds, and the one death in this group was an infant whose mother was Rh-, father Rh+. Weight was 4 pounds, 1 ounce. The infant was transfused with 20 c.c. of Rh- blood from a professional donor. The baby did well until the second day, when it began to show signs of cerebral hemorrhage and died the following day; autopsy revealed a massive cerebral hemorrhage.

The results in these cases may be compared with Stander's mortality figures for premature infants: 100 per cent for weight less than 1,000 grams, 65.6 per cent from 1,000 to 1,500 grams, and 25 per cent from 1,500 to 2,000 grams.³ They may also be compared with Holt and McIntosh's figures for prematures under ideal hospital conditions: 95 per cent for weight less than 1,000 grams, 67 per cent from 1,000 to 1,500 grams, and 25 per cent from 1,500 to 2,000 grams. The mortality rate for prematures at the Methodist Hospital, 1940 through 1943, all weights under 5½ pounds, including these 18 cases, was 22.8 per cent (81 deaths among 354 living prematures).

TABLE II. CORD TRANSFUSIONS IN 18 INFANTS WEIGHING LESS THAN 5½ POUNDS

| WEIGHT POUNDS OUNCES | | GESTATION | AMOUNT OF BLOOD | REMARKS |
|-------------------------|----|-----------|--------------------|--|
| 1 | 6 | 23 weeks | 20 c.c. | Died in 35 minutes. Nonviable. |
| 2 | 7 | 26 weeks | 30 c.c. | Hb. 21.7 Gm., reds 6,280,000 at birth. At 6 months weighed 11 pounds. |
| 2 | 14 | 28 weeks | 15 c.c. | Critical at birth, respirations intermittent, periods of apnea. |
| 2 | 15 | 32 weeks | 30 c.c. | Died at 3 months of strangulated hernia. Not a neonatal death. |
| 3 | 2 | 28 weeks | 30 c.c. | Color poor, prognosis guarded. |
| 3 | 9 | 34 weeks | 20 c.c. | Hb. 22.4, reds 6,000,000. Critical. Hb. 150%, reds 6,200,000. At one month weighed 5 pounds 5 ounces. |
| 3 | 11 | 32 weeks | 30 c.c. | Died within 15 hours. Critical, breech. Blood aspirated from throat. |
| 3 | 12 | 33 weeks | 35 c.c. | One of twins. Red cells 7,500,000. Other twin, 5,500,000. |
| 3 | 13 | 33 weeks | 20 c.c. | Mother Rh+, father Rh-. |
| 4 | 1 | 32 weeks | 20 c.c. | Critical at birth. Discharged in 25 days weighing 5 pounds 4 ounces. |
| 4 | 1 | 36 weeks | 20 c.c. | Died on the third day. Mother Rh-, father Rh+. Blood from professional donor used. Autopsy showed massive cerebral hemorrhage. |
| 4 | 3 | 32 weeks | 35 c.c. | Apparently about 6 months' gestation. Critical at birth. |
| 4 | 4 | 28 weeks | 40 c.c. | Mother had lost two premature infants. Father's blood used. |
| 4 | 6 | 33 weeks | 20 c.c. | Critical for several days. |
| 4 | 13 | 32 weeks | 30 c.c. | Hb. 19 Gm., reds 8,000,000. Previous delivery by cesarean. |
| 4 | 14 | 36 weeks | 20 c.c. | Spontaneous delivery. Fair at birth. |
| 4 | 14 | 39 weeks | 20 c.c. | Mother toxic. Red cells 7,500,000 Twin. Hb. 16 Gm., reds 7,050,000, 35% nucleated red cells. In 6 days Hb. 16.5 Gm., reds 5,000,000, occasional nucleated red cell. |
| 5 | 5 | 36 weeks | 18 c.c. | Hb. 24 Gm., reds 6,550,000. |

NOTE: In several of the above cases the transfusion should have been larger. This is especially evident in the case of the 4-pound, 1-ounce infant, mother's blood Rh-. A transfusion of 40 or 45 c.c. might have saved this baby.

TABLE III. TOTAL CORD TRANSFUSIONS

| | TOTAL | LIVED | DIED | REMARKS ON DEATHS |
|--------------------|-------|-------|------|---|
| Under 2 pounds | 1 | | 1 | Lived 35 minutes. Nonviable. Weight 1 pound 6 ounces. Given 20 c.c. mother's blood. |
| 2 to 3 pounds | 3 | 3 | | |
| 3 to 4 pounds | 5 | 4 | 1 | Lived 15 hours. 32 weeks. Breech. Critical at birth. Given 30 c.c. mother's blood. Blood aspirated from throat. |
| 4 to 5½ pounds | 9 | 8 | 1 | Lived 3 days. Mother Rh-, father Rh+. 20 c.c. blood from Rh- professional donor used. Autopsy showed massive cerebral hemorrhage. |
| 5½ pounds and over | 16 | 15 | 1 | Lived 25 minutes. Weight 6 pounds, 4 ounces. 36 weeks. Both parents Rh+. Autopsy showed hemorrhagic disease of the newborn. |
| Total | 34 | 30 | 4 | |

NOTE: There were 31 viable babies transfused with mother's blood with only one death.

Case Reports

CASE 1.—Mrs. D. A. had lost two babies, one at 8 months' gestation which lived for 12 hours, another at 7 months which lived for 5 hours. There was no autopsy in either case; cause of death was given as prematurity and atelectasis.

Mrs. D. A. was admitted to the Methodist Hospital on September 1, 1940, in active labor. Gestation was 7 months. No sedatives were given and only a small amount of nitrous oxide for the delivery. The baby weighed 4 pounds, 4 ounces at birth, and 40 c.c. of the father's blood were given by cord transfusion. The infant lived, and now at the age of 3 is a normal child.

(For fourth child, see Case Report 3.)

CASE 2.—Mrs. A. W. was admitted to the hospital October 16, 1941. She was a para i, aged 37. Gestation was only 26 weeks. Delivery was breech, birth weight 2 pounds, 7 ounces, red cells 6,280,000, Hb. 128 per cent, baby's condition at birth critical. Thirty cubic centimeters of mother's blood were given by cord transfusion. The infant was discharged from the hospital January 2, 1942, weighing 5 pounds, 2 ounces. At the age of 6 months weight was 11 pounds. This is the smallest baby in the series of prematures to survive.

In 1943, cord transfusions were given to full-term infants as well as to prematures. In the 16 infants weighing 5½ pounds and over and classed as full terms, the indications for cord transfusion were: difficult forceps deliveries, 10; difficult breech extractions, 3; previous loss of infant, 2; twin, 1. There was one death in this group. A previous premature had survived, the first in the series of 18 prematures given cord transfusions; two prematures before that had died. This infant weighed 6 pounds, 4 ounces, gestation 36 weeks, thus a premature in spite of size. Twenty cubic centimeters of father's blood were given, but the infant lived only 25 minutes; autopsy revealed death from hemorrhagic disease (Case Report 3, Mrs. D. A.).

Mother's blood was given in 15 cases, father's blood, in which the death occurred, in 1.

CASE 3.—Mrs. D. A. For previous history see Case Report 1.

This mother had her fourth child in June, 1943. Gestation was 36 weeks, weight 6 pounds, 4 ounces. The infant was transfused with 20 c.c. of its father's blood, but lived only 25 minutes. Autopsy showed it died from hemorrhagic disease. Both parents were Rh+.

CASE 4.—Mrs. M. D. had lost two babies, both full term. The first died during delivery; the cord smear showed 30 per cent normoblasts. The second had been transfused (not a cord transfusion) with 50 c.c. of its father's blood but lived for only 36 hours. This infant also had 30 per cent normoblasts in the cord blood.

On August 18, 1943, this patient was delivered of a baby weighing 6 pounds, 14 ounces. There were 73 per cent normoblasts in the cord blood. It was given 40 c.c. of mother's blood by cord transfusion. On the fifth day the normoblasts were only 5 per cent. The infant made an uneventful recovery. Both parents were Rh+.

Technique

The administration of blood by way of the umbilical vein is a very simple procedure. The citrated blood to be given should be in readi-

ness before the baby is delivered. A 50 c.c. syringe is used in which are 5 c.c. of a 2 per cent solution of sodium citrate. The blood is withdrawn and the syringe tilted several times to mix the citrate solution with it. If the mother is toxic, or if for any other reason her blood is not desirable, blood from the father, some other donor or from the bank if it is available may be used. Preserved blood should be filtered through several layers of gauze before being administered.

As soon as the baby is born and before cutting the cord, the umbilical vein is easily identified and may be entered with the same needle used to withdraw the blood. If preferred a cannula may be placed in the vein. The transfusion should be started as far from the baby as possible. This serves two purposes: if the vein is not easily entered another attempt can be made nearer the baby; if the baby should move the needle will not be disturbed. As soon as the transfusion is started the cord should be clamped between the needle and the placenta. If it is decided to cut the cord before giving the transfusion, the cord may be gently compressed with the fingers near the umbilicus so that the veins remain distended until the transfusion is started.

The transfusion should be given slowly, 30 or 40 c.c. in about five minutes. If the operator is dubious about embarrassing the child's circulation with too many erythrocytes, as soon as the baby is delivered the cord is clamped so as not to allow the placental blood to enter the baby, since the amount of placental blood that could be milked into the baby from the cord would amount to as much as or more than that given by the transfusion, and the transfusion is then started.

If there is any delay, as in drawing the blood from the donor or in starting the transfusion, it may be impossible to get the blood to flow through the cord. If there has been considerable trauma to the cord during delivery, transfusion via the cord may be impossible.

There has been some discussion as to the amount of blood that should be given. For premature infants, in whom the purpose of the transfusion is to provide a medium for the carrying on of the circulation, a considerable amount would seem to be indicated, and pediatricians recommend 15 to 20 c.c. per kilogram of baby weight. As much as 150 c.c. may be given a full-term baby if it has had a hemorrhage or if it is suffering from hemorrhagic disease of the newborn. Such large transfusions may cause some cyanosis, but otherwise do not seem to affect the infant. In our series of prematures in a number of cases we felt that more blood might have been given, and in one case at least might have saved the life of the child.

A striking phenomenon occurring during cord transfusions, the cause of which is still to be investigated, is the blanching of the cord during the transfusion, the veins apparently collapsing.

Rationale of the Method

When a baby is premature, it often seems, at first, like a normal but small infant. The color is good; the cry and the respirations are usually spontaneous. The obstetrician, thinking the infant will survive, orders premature care, shifting responsibility to the pediatrician, who may not see the child for twelve or even twenty-four hours after delivery. A few hours after delivery the baby becomes cyanotic, its condition critical, and death ensues.

In prematurity, nature has not had sufficient time to complete preparations for extrauterine life. It may be assumed that the immature red corpuscles are not accustomed or able to gather the oxygen from the lungs, carry it to the body tissues and bring back the carbon dioxide and release it in the lungs. This fact may very well account for the early cyanosis. The use of any stimulation, clyses or the administration of oxygen has little effect in the premature infant. But the administration of adult blood immediately following delivery, by way of the umbilical vein, gives the infant an adult tissue that enhances the baby's chances for survival because the blood not only acts as nourishment, but also stimulates respiration and helps to overcome cyanosis. In the premature, the need for nourishment and stimulation in the first few hours after birth is urgent.

One of the most serious difficulties for premature infants is hemorrhage. Porter and Carter,⁴ and Holt and McIntosh claim that many premature infants and almost all of those weighing under 1,000 grams suffer from intracranial bleeding. According to Holt and McIntosh, the fragility of the blood vessels is greater than in the full-term infant, and the concentration of prothrombin less. Porter and Carter believe that a deficiency of vitamin K and of prothrombin storage during fetal life is closely associated with hemorrhagic disease in the newborn infant. Before the administration of vitamin K to all patients in labor was adopted at the Methodist Hospital, it had been our routine practice when a delivery was extremely difficult to give the infant blood subcutaneously to forestall any tendency to hemorrhage. It would seem that in hemorrhage or tendency to hemorrhage occurring in spite of the vitamin K administration, if subcutaneous injection of blood would be of assistance, intravenous transfusion of blood would have even more benefit.

When blood is given to the newborn infant which shows some evidence of shock with poor respirations, it is surprising how often the respirations are stimulated after the cord transfusion. The time at which change in respiratory rate takes place seems to correspond to the time it would take the blood to reach the respiratory center. In adults, the effect of transfusions of blood or plasma in shock with or without hemorrhage is well recognized.

Prompt transfusion is most important in infants suffering from erythroblastosis. The number of normoblasts may be only slightly increased at birth, but unless transfusion is done at once, they multiply very rapidly and repeated transfusions may be needed to save the life of the child.

According to Levine et al.,⁵ if the mother gives a history of stillbirths, miscarriages or of infants dying soon after delivery, tests for the Rh factor should be carried out early in pregnancy so that at the time of delivery if the mother is Rh negative, the infant may be transfused with blood from an Rh- compatible donor.

So far as the question of compatibility is concerned, Levine, in a personal communication,⁶ states as follows:

"With regard to compatibility tests it is significant that the newborn infant's blood contains no isoagglutinins characteristic of its blood group. Any agglutinins which are demonstrable are derived from the mother. Accordingly, one transfusion may be given without resorting either to blood grouping or to compatibility tests. Should the mother's blood be incompatible, it is certain that the blood will survive long enough to exert its beneficial effect on the newborn infant. However, this transfusion serves to immunize the infant so that the following transfusions, if required, must be carried out with compatible blood of the same blood group as the infant's. Although the mother's blood may be given indiscriminately for one transfusion, it seems preferable to use any blood of group O.

"As already indicated [reference to Levine et al.] the erythroblastotic infant of an Rh negative mother should be transfused with random Rh negative blood which is otherwise compatible."

Comparison may be made among the infants in three sets of twins, two in the premature series, one in the full term. In each set the second twin was transfused. In the two transfused infants from the premature series the red cells were about 2,000,000 higher than in the untreated mate and the hemoglobin correspondingly higher. In addition one of these transfused twins (weight 4 pounds, 14 ounces, 39 weeks' gestation) had 35 per cent normoblasts in its blood, while its mate had only an occasional nucleated red cell. In six days in this infant the count was normal, and the red cells dropped from 7,050,000 to 5,000,000. In the other treated twin, however (weight 3 pounds, 12 ounces, gestation 33 weeks, red cells at birth 7,000,000), the red cells six days later were still 7,000,000.

All of the babies lived, but in each case the transfused infants were much more active. There was little difference in their gain in weight.

Discussion

I have been unable to find any mention in the literature of the umbilical cord as an avenue for the routine transfusion of the baby in the delivery room. Sidbury⁷ in 1923 reported a case in which the attending physician had done a dorsal slit on an infant, and it had bled for four days. A wet dressing of boric acid was applied to the cord, and eight hours later the cord was cut proximal to the ligature, a regular transfusion needle was inserted into the umbilical vein and when no resistance was felt on the injection of saline, 100 c.c. of mother's blood were transfused. As far as Sidbury knew this method had never been used before. Marriott,⁸ 1936, states: "In infants of two days old, particularly when suffering from hemorrhagic disease, the umbilical vein may be entered quite readily after removing the ligature around the cord."

For simplicity the method has no comparison with any other method of giving transfusions to newborn infants. It is possible for one skilled in using the scalp veins to do such transfusions in some infants, but in many the veins are small and difficult to enter, and it is even more difficult to keep the needle in the vein long enough to give the required amount of blood. In desperation the physician will endeavor to give the blood by way of the longitudinal sinus. The location of the sinus is not constant, and not infrequently the blood is given subdurally and death of the infant results.

In a paper published in 1924, I⁹ described a method of transfusing newborn infants by way of the median basilic vein, and during the next twelve years more than 100 such transfusions were given. It was found that when the transfusions were given early, the infant usually lived, mortality increasing with the number of days of delay. Transfusions given the day following delivery may be too late to save the baby, and they may be even further delayed by search for a compatible donor and waiting for a convenient time when a physician experienced in transfusing infants may give the transfusion.

In defining prematurity, we are confronted with many borderline cases. On the basis of weight alone some infants are classified as prematures when actually they are full term or nearly so. An example is the twin in the series of 18 prematures, weight 4 pounds, 14 ounces, gestation 39 weeks. Such babies usually survive. On the other hand, there are the infants that, judged by weight, are classified as full term whereas on the basis of gestation they are really premature. Among the 16 "full-term" infants given cord transfusions, 3 had a gestation of 36 weeks or less, and the only one in the series to die was of this type. Weights at full term in such infants might have been eight, nine, even eleven pounds, and the question arises as to the probable weight at seven months' gestation of an infant weighing eleven pounds at term. In the case of these infants we are likely to ignore the possibility of prematurity, fail to order premature care, and the infants die. Such infants should always be treated as prematures, and cord transfusion as a prophylactic procedure should apply equally to large and small prematures.

The method suggests usefulness in salvaging prematures delivered by cesarean section. In 1943 at the Methodist Hospital 9 cesarean sections were done while the infant was premature. The smallest weighed 3 pounds, 2 ounces, the largest 5 pounds, 7 ounces. Five of these babies died, a mortality of 55 per cent. None was transfused. Although cesarean sections are frequently done solely in the interest of the premature infant, such infants are often lost.

Summary

The umbilical vein offers a convenient avenue by which newborn infants may be transfused with adult blood in the delivery room im-

mediately after birth. Citrated mother's blood has been used in most cases to date; father's or donor's blood or blood from the bank may serve as a substitute. A little less than 10 c.c. per pound of baby weight is sufficient. The technique is simple.

Premature infants and particularly those usually considered non-viable are definitely benefited.

In infants suffering from difficult delivery and those in doubtful condition, a small transfusion of 20 c.c. of mother's blood acts as a direct stimulation to the respiratory center and tends to overcome any tendency toward hemorrhage.

If the mother gives a history of previous stillbirths or if hemorrhagic disease or erythroblastosis is suspected, cord transfusions may be of benefit.

Thirty-four cases of cord transfusion are reported, 18 in infants weighing less than 5½ pounds, gestation from 23 to 39 weeks, 16 in infants weighing 5½ pounds and over, 13 full term, 3 with gestation of 36 weeks or under. There were 4 deaths, 3 in the smaller weight group, 1 in the larger.

This is a preliminary report of a simple, apparently harmless procedure which may be the means of saving more premature babies, of benefiting full-term infants when the delivery has endangered life, and of treating the blood dyscrasias.

The writer wishes to express his gratitude to Dr. Philip Levine for his personal note and for his helpful suggestions in the editing of this paper. The majority of the cord transfusions were done by Dr. Everado Goyanes and Dr. Isabel Seissman, our residents in obstetrics.

Note.—There were 24 additional cord transfusions during the first 2½ months of 1944. Nine of the babies were premature, with two deaths. The mother of one had a premature separation of the placenta and the baby lived for 5 hours. The other lived for 4 days following a breech delivery, accidental hemorrhage was from a low implantation of the placenta; the cause of death was intracranial hemorrhage. There were 15 babies weighing more than 5 pounds, 8 ounces. To date, the total number of cord transfusions is 58, with six deaths.

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THE PROGNOSIS AND MANAGEMENT OF PREMATURE RUPTURE OF THE MEMBRANES*

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THERE have been several papers written in the past decade which emphasized the fact that premature rupture of the membranes is not a complication of obstetrics and therefore, the so-called "dry labor" is not a condition to be feared. However, because dry labor was so emphasized in the past and because many of the textbooks are slow in adapting the newer concept, it may be well to review again a series of cases showing the results which have occurred following premature rupture and thereby draw some conclusions as to the proper management of this condition.

Material

In order to secure a representative group of patients the cases used in this series were taken from two hospitals: First, a large maternity hospital, the staff of which consists of men trained and specializing in obstetrics and gynecology; and second, a smaller general hospital with an obstetrical staff but with many general practitioners doing "occasional obstetrics." Both ward and private patients were used to eliminate variation in economic, physical and nutritional factors. The cases used were all women delivered in these two hospitals from Jan. 1, 1942, to July 1, 1943.

TABLE I

| | |
|--|-------|
| Total number of patients delivered | 4,806 |
| Total number of infants | 4,859 |
| Total number of patients with premature rupture of the membranes | 636 |
| Total number of infants | 645 |

The total number of patients delivered in these two institutions during this period was 4,806. There were 53 sets of twins resulting in a total of 4,859 infants. Of these patients, 636 or 13.2 per cent had definite rupture of the membranes before the onset of labor pains. It is unreliable to use this as an absolute incidence because the diagnosis of rupture of the membranes was based on clinical evidence alone. Other cases probably had ruptured membranes but were discarded because their histories were not definite. This series also includes 12 cases of artificial rupture performed for induction of labor.

Of these 636 patients, 117 or 18.4 per cent began to have labor pains within an hour of the time of the rupture of the membranes. In these cases rupture of the membranes was probably the initial sign of the onset of labor. The majority of patients began to have labor pains within

*Read at a meeting of the Philadelphia Obstetrical Society, March 2, 1944.

1 to 6 hours of the time of rupture of the membranes. Twenty patients had a latent period of more than 72 hours before the onset of labor, the longest latent period being 63 days.

TABLE II. PERIOD OF TIME BETWEEN RUPTURE OF THE MEMBRANES AND THE ONSET OF LABOR

| LATENT PERIOD | NO. OF PATIENTS | % | NO. OF INFANTS |
|----------------|-----------------|------|----------------|
| 0 to 1 hour | 117 | 18.4 | 119 |
| 1 to 6 hours | 262 | 41.2 | 267 |
| 6 to 12 hours | 112 | 17.6 | 113 |
| 12 to 24 hours | 77 | 12.1 | 78 |
| 24 to 48 hours | 34 | 5.3 | 34 |
| 48 to 72 hours | 14 | 2.2 | 14 |
| Over 72 hours | 20 | 3.1 | 20 |
| Total | 636 | | 645 |

The factors most feared in the management of patients with premature rupture of the membranes have been (1) prolongation of the first and second stages of labor, (2) increased incidence of operative deliveries, (3) sepsis and (4) injury to the fetus.

Length of Labor

TABLE III

| | NORMAL | MEMBRANES RUPTURED | MEMB. RUPT. OVER 24 HR. | OCCIPUT POST. | BREECH |
|------------|----------|--------------------|-------------------------|---------------|----------|
| Primiparas | 18.0 hr. | 11.6 hr. | 11.4 hr. | 16.2 hr. | 12.0 hr. |
| Multiparas | 12.5 hr. | 7.9 hr. | 9.6 hr. | 12.3 hr. | 7.0 hr. |

Textbooks quote the average length of labor as eighteen hours for primiparas and twelve and a half hours for multiparas. In this series the patients with ruptured membranes averaged 10.2 hours for the first and second stages of labor, 11.6 hours for primiparas and 7.9 hours for multiparas. It might be expected that labor would be lengthened to a greater degree in patients with occiput-posterior positions and breech presentations but even these patients had a shorter labor than the normal usually quoted. It is difficult to compare these findings with the stated normal length of labor because in both institutions the use of prophylactic forceps is routine, thereby shortening the second stage of labor, but it is safe to conclude that labor is not lengthened by premature rupture of the membranes.

In the 68 cases with membranes ruptured over 24 hours before the onset of labor, the average length of the first and second stages of labor was 11.4 hours for primiparas and 9.6 hours for multiparas. Therefore, there does not seem to be any relationship between the length of the latent period before the onset of labor and the length of labor.

These observations serve to invalidate the theory that the bag of waters is necessary for efficient dilatation of the cervix. If this concept was true, then premature rupture of the membranes would certainly result in a lengthening of the first stage of labor. DeLee and Greenhill

state in their textbook that the best time for the membranes to rupture is when the cervix is completely dilated and effaced, but this does not seem to be justified. The unruptured membranes probably bulge into and through the dilating cervix because this is the point of least resistance rather than having any hydrostatic action.

Incidence of Operative Deliveries

TABLE IV

| OPERATIONS | TOTAL SERIES | % | RUPTURED MEMBRANE | % |
|------------------------|-----------------|------|----------------------|------|
| Forceps | 2,794 | 57.5 | 401 | 62.1 |
| Low | 2,601 | 53.5 | 383 | 59.2 |
| Mid | 188 | 3.8 | 18 | 2.8 |
| High | 5 | 0.1 | 1 | 0.1 |
| Breech extraction | 123 | 2.5 | 16 | 2.4 |
| Version and extraction | 31 | 0.6 | 5 | 0.7 |
| Cesarean section | 268 | 5.5 | 7 | 1.0 |
| Total operations | 3,216 | 66.1 | 429 | 66.4 |

The incidence of operations in the total series and in the group with premature rupture of the membranes was almost identical. There was a slight increase in the incidence of low forceps operations in the group with ruptured membranes. The incidence of cesarean section was greater in the total group, as might be expected since many of these cases in this group were elected at some time before the expected date of delivery allowing less opportunity for rupture of the membranes. The indications for the seven cesarean sections performed on the patients with premature rupture of the membranes were as follows:

1. Large breech. Membranes ruptured before elective section. No labor.
2. Disproportion. Membranes ruptured before elective section. No labor.
3. Previous cesarean section.
4. Cervical dystocia.
5. Premature rupture of the membranes given as the indication. Failure of several attempts at medical induction and surgical induction with bag. Porro section.
6. Fibroid obstructing delivery.
7. Disproportion. Eight-hour test of labor.

In only one of these cases was premature rupture of the membranes thought to be a factor inhibiting normal progress.

An analysis of the patients with premature rupture of the membranes reveals that there were no more complications of labor than might be expected in any large series of cases. When the membranes rupture before the onset of labor, they probably do so only when the presenting part is able to descend far enough to exert pressure upon the forewaters. When this occurs, there is little room for prolapse of the cord which can take place only when the presenting part is poorly adapted to the inlet of the pelvis. This concept is confirmed by the fact that there were no cases of prolapse of the cord among the 636 patients with premature rupture of the membranes.

Maternal Morbidity

The maternal morbidity rate for the entire series of 4,806 cases was 7.3 per cent. The maternal morbidity rate for the 636 patients with premature rupture of the membranes was 5.1 per cent indicating that premature rupture of the membranes does not result in increased morbidity. This is even more evident when the causes for maternal morbidity are analyzed.

TABLE V. CAUSES OF MATERNAL MORBIDITY

| | |
|-----------------------------|-----------|
| Pyelitis | 9 |
| Cystitis | 1 |
| Retained secundines | 1 |
| Endometritis | 7 |
| Septicemia | 1 |
| Infected perineum | 1 |
| Upper respiratory infection | 1 |
| Aspiration pneumonia | 1 |
| Postoperative reactions | 3 |
| Unknown | 8 |
| | <u>33</u> |

Pyelitis, cystitis and respiratory infections cannot be associated with premature rupture of the membranes allowing a correction of the morbidity rate to 3.3 per cent. This increases the validity of the assumption that premature rupture of the membranes does not cause an increase in maternal morbidity.

TABLE VI. MORBIDITY IN RELATION TO THE LATENT PERIOD

| LATENT PERIOD | NO. OF CASES | MORBID | % |
|----------------|--------------|--------|-----|
| 0 to 1 hour | 117 | 10 | 8.5 |
| 1 to 6 hours | 262 | 10 | 3.9 |
| 6 to 12 hours | 112 | 5 | 4.4 |
| 12 to 24 hours | 77 | 6 | 7.9 |
| 24 to 48 hours | 34 | 1 | 3.2 |
| 48 to 72 hours | 14 | 0 | 0.0 |
| Over 72 hours | 20 | 1 | 5.0 |
| Total | 636 | 33 | 5.1 |

As can be seen in Table VI, the maternal morbidity rate was greatest in the group of patients whose membranes had been ruptured less than one hour, and there was no increase in morbidity in relation to the increase of the latent period. Only two of the 68 patients with a latent period of 24 or more hours were morbid; one of these was due to pyelitis, and the other to endometritis. Only one of the 34 patients with a latent period of 48 or more hours was morbid and this was due to pyelitis. The most serious post-partum infection, septicemia, occurred in a patient whose membranes had been ruptured only 1.5 hours before the onset of labor and whose labor had lasted 2 hours and 38 minutes. It is therefore obvious, that with ordinary precautions puerperal infections do not result in spite of the membranes having been ruptured over long periods of time before the onset of labor.

Infant Mortality

TABLE VII

| LATENT PERIOD | NO. OF INFANTS | STILLBIRTHS | % | NEONATAL DEATHS | % |
|------------------------|-------------------|-------------|------|--------------------|------|
| 0 to 1 hour | 119 | 0 | | 0 | |
| 1 to 6 hours | 267 | 1 | | 2 | |
| 6 to 12 hours | 113 | 1 | | 3 | |
| 12 to 24 hours | 78 | 0 | | 0 | |
| 24 to 48 hours | 34 | 3 | | 0 | |
| 48 to 72 hours | 14 | 0 | | 0 | |
| Over 72 hours | 20 | 2 | | 2 | |
| Total | 645 | 7 | 1.10 | 7 | 1.10 |
| Total in entire series | 4,859 | 92 | 1.89 | 94 | 1.97 |

There was a slight decrease in both the stillbirth rate and the neonatal death rate of the cases with premature rupture of the membranes. This difference is probably a significant one, certainly there is no evidence that the life of the infant is jeopardized by a "dry labor."

There was an increase in the number of premature infants in the group of cases with premature rupture of the membranes, 40 in the series of 645 infants. Most of these premature infants were well beyond the viable stage, prematurity being the cause of only 2 infant deaths. There is no evidence in this data to indicate whether premature rupture of the membranes was responsible for the high percentage of premature infants, or whether the membranes ruptured as the initial sign of impending premature labor from some other cause.

Management

It is evident from the above statistical review that the best management of premature rupture of the membranes consists primarily of waiting for the patient to go into labor, difficulties arising only when "meddlesome obstetrics" is initiated. When there is conclusive evidence that the membranes have ruptured, it is best to hospitalize the patient in order that she may be kept under aseptic conditions and constant observation. It is open to question whether this is necessary with intelligent patients since a large number included in this series remained at home and carried on their domestic activities for varying periods of time without bad results. It seems probable that patients are safe from infection unless there is the introduction of some nonsterile object into the lower genital tract.

When the patient is near term, medical induction consisting of castor oil and/or an oxytocic drug may be initiated. Even this is not indicated except for the doubtful reasons of economics or convenience.

Since premature rupture of the membranes should not be considered a complication of late pregnancy, the management of this condition is a relatively simple one.

Conclusions

1. Spontaneous premature rupture of the membranes shortens the duration of the first and second stages of labor.
2. There is no increase in the incidence of operative deliveries.
3. Premature rupture of the membranes usually takes place when the feto-pelvic relationship is favorable enough for the presenting part to enter the pelvis early and easily.
4. There is no increase in the maternal morbidity rate, even in those cases with ruptured membranes for long periods of time before the onset of labor.
5. Premature rupture of the membranes does not jeopardize the life of the infant.
6. Management of premature rupture of the membranes consists of maintaining aseptic precautions and, either inducing labor if the patient is near term, or waiting for the patient to go into labor spontaneously.

I wish to thank the members of the staffs of the Philadelphia Lying-in and the Methodist Hospitals for the privilege of using the records of their private patients which have been included in this paper.

3400 QUEEN LANE

Discussion

DR. ROY MOHLER.—Dr. Bishop's presentation has shown how frequently premature rupture of the membranes occurs in obstetric practice. The incidence of 13.2 per cent which he has stated is probably lower than the absolute incidence since the observation of premature rupture of the membranes was based entirely upon simple clinical evidence. Why premature rupture of the membranes occurs so often has not been explained satisfactorily, but it is an incident in pregnancy which is very important, and until very recently was cited as a definite cause for dystocia.

This presentation has shown that the mean length of labor was shorter in the patients who ruptured their membranes before labor began, than the stated standards for the length of labor and, that the incidences of sepsis and injury to the fetus were not increased because of the incident. These observations are very important, and tend to controvert a generally accepted impression that the early rupture of the membranes was an unfortunate event which would likely increase the normal hazard of labor for the mother and child.

In the past decade, most of us have begun to sense from our experience with the use of artificial rupture of the membranes as a means of inducing labor in selected cases, that it was innocuous, and that the dangers previously ascribed to the incidence were probably mistaken concepts. We know now from this report and other recent observations, that rupture of the membranes does not inhibit the progress of normal labor, and in many circumstances, that it actually facilitates labor. Dr. Bishop's statistical report actually confirms the clinical impression that labor can often be facilitated by artificial rupture of the membranes at certain periods during the progress of normal labor.

I think the facts which have been stated in this presentation are generally appreciated by those who are active and observing in obstetric work. There has been so much adverse sentiment developed against the phenomenon known as premature rupture of membranes, both in the literature and textbooks, that much data will have to be collected and reported before the correct concept will be generally accepted.

DR. CHARLES A. BEHNEY.—Dr. Joseph MacFarland once remarked that it is better to be uninformed than to know something that is not true. This is particularly pertinent with regard to the teaching in textbooks and classrooms regarding premature rupture of the membranes. It has been demonstrated repeatedly by Plass and others that premature rupture of the membranes (dry labor) *per se* does not increase the duration of labor. Premature rupture of the membranes is usually found to occur more frequently when there is an abnormal presentation, or in connection with disproportion, so that if the cases of premature ruptured membranes are compared with those in which the membranes remain intact until shortly before birth, the former group will usually have longer labors. If, however, the patients with normal presentations and prematurely ruptured membranes are compared with those normal presentations in which the membranes are not ruptured prematurely, it will be found that the normal presentations with premature rupture of the membranes are in labor, on an average, a shorter time than those without premature rupture of the membranes. Furthermore, in abnormal presentations the patients with prematurely ruptured membranes deliver sooner, on an average, than the ones in which premature rupture of the membranes has not occurred. Premature rupture of the membranes before engagement of the head, increases the danger of prolapsed cord. Artificial rupture of the membranes after the head is engaged does not predispose to prolapse of the cord.

Dr. Bishop's conclusions are in entire accord with the reports of most of other investigators of this condition. I am convinced that artificial rupture of the membranes in carefully selected cases is good practice. In toxemia, it is an important prophylactic measure.

DR. J. TOLAND.—I must confess that I still carry a slight chip upon my shoulder on account of the incorrect teaching I received on the point of premature rupture of the membranes during my medical-student and intern days. As my experience increased I found, as I am sure have the other members of this Society, that far from being a calamity, that the premature rupture of the membranes in the vast majority of cases was the welcome herald of a short labor and I still begrudge the anxiety that I felt in my early days, on account of previous erroneous teaching.

DR. BISHOP (closing).—First, in answer to Dr. Vaux. Although some of the patients do get into trouble, I probably was fortunate in my series. I know that in other series, cases of prolapse of the cord have been reported, but most of these followed artificial rupture rather than spontaneous rupture. I feel that spontaneous rupture is a naturally selective procedure. The presenting part is probably fitting well into the pelvis and the labor will probably proceed well. It may be that these patients have done better because they have been more closely watched. That is probably the reason for the decrease in morbidity rate.

Second, in answer to Dr. Sharkey. There have been some cases considered by the maternal mortality committee in which premature rupture of the membranes has been a factor. In 1940, 1941 and 1942, there were 11 such cases. Death in three of these was due to hemorrhage, one to embolism, and three to endocarditis. The endocarditis in each case was the result of heart disease which had pre-existed for a long period of time. The remaining four had septic deaths, but in three "meddlesome obstetrics" was a factor. These patients died, not because they had premature rupture of the membranes, but because it was considered a complication and unwarranted interference was instituted.

THE CLINICAL SIGNIFICANCE OF MIDPLANE PELVIC CONTRACTION*

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THE determination of certain pelvic diameters and the consideration of pelvic morphology is definitely useful in estimating pelvic capacity in its relation to childbirth. In the living individual this information can be readily secured roentgenologically and views made from the superior and from the lateral aspects of the pelvis will enable the observer to study pelvic morphology readily and to determine with essential accuracy the important linear measurements.

There are three portions of the pelvis which are important in such a pelvimetric survey; these are the pelvic inlet, the midpelvic plane and the pelvic outlet. It has been known for a long time that any or all of these portions of the bony pelvis may show a relative diminution in area, but only until comparatively recently has emphasis been made upon the importance of midplane contraction in its relation to labor. Hanson's paper¹ on the transversely contracted midpelvis, published in 1936, is an important landmark.

For the purpose of the present discussion the important pelvic diameters may be reviewed, as follows (see Figs. 1 and 2):

| | |
|--------------|---|
| PELVIC INLET | Anteroposterior, transverse, posterior sagittal |
| MIDPLANE | Anteroposterior, transverse, posterior sagittal |
| OUTLET | Widest transverse diameter, bituberal† |

Some idea of the average ranges for these diameters may be gained from the accompanying table, in which the findings of 500 women have been summarized.²

| | AVERAGE DIAMETER RANGE IN 500 PELVES | | |
|--------------------|--------------------------------------|---------------|----------------|
| | DOLICHOPELLIC | MESATYPELLIC | BRACHYPELLIC |
| INLET | | | |
| Anteroposterior | 12.0 to 13.0 | 11.5 to 12.25 | 10.5 to 11.5 |
| Transverse | 11.5 to 12.25 | 12.0 to 12.75 | 12.25 to 13.25 |
| Posterior sagittal | 4.5 to 5.5 | 4.25 to 5.0 | 4.0 to 4.5 |
| MIDPLANE | | | |
| Anteroposterior | 12.0 to 13.0 | 11.75 to 13.0 | 11.5 to 12.75 |
| Transverse | 9.25 to 10.25 | 10.0 to 10.75 | 10.0 to 11.0 |
| Posterior sagittal | 4.75 to 5.5 | 4.5 to 5.5 | 4.5 to 5.5 |
| OUTLET | | | |
| Widest transverse | 11.3 | 11.9 | 12.0 |

*This study was made possible through grants from the Clinical Research and Teaching Funds of the Yale University School of Medicine.

†We measure the bituberal manually.

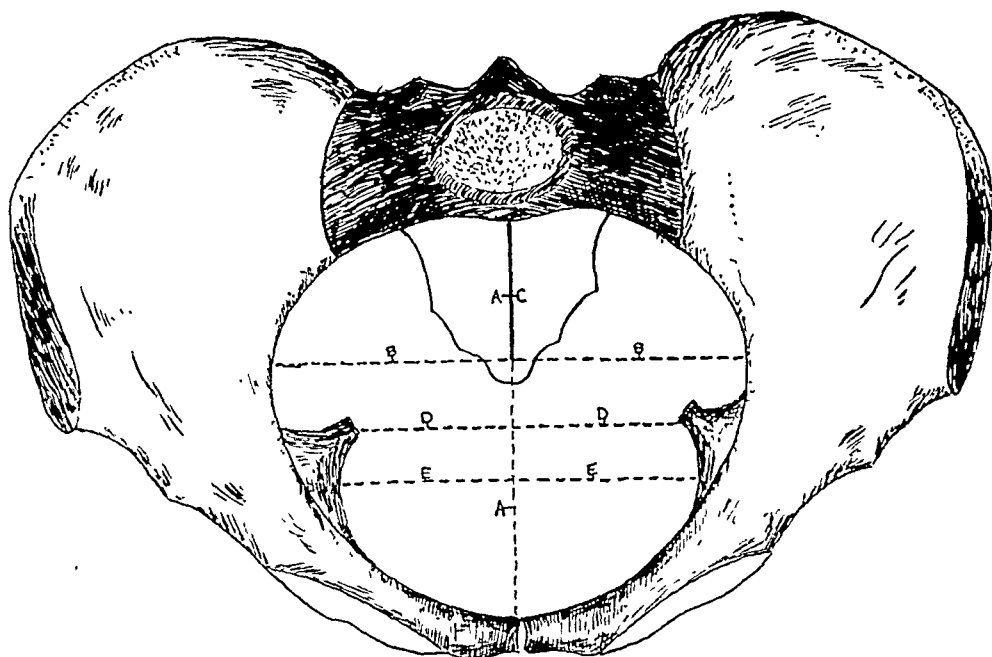


Fig. 1.—The pelvis seen from above. *A*, Anteroposterior diameter of inlet; *B*, transverse diameter of inlet; *C*, posterior sagittal diameter of inlet; *D*, interspinous or transverse diameter of midplane; *E*, widest transverse diameter of outlet.

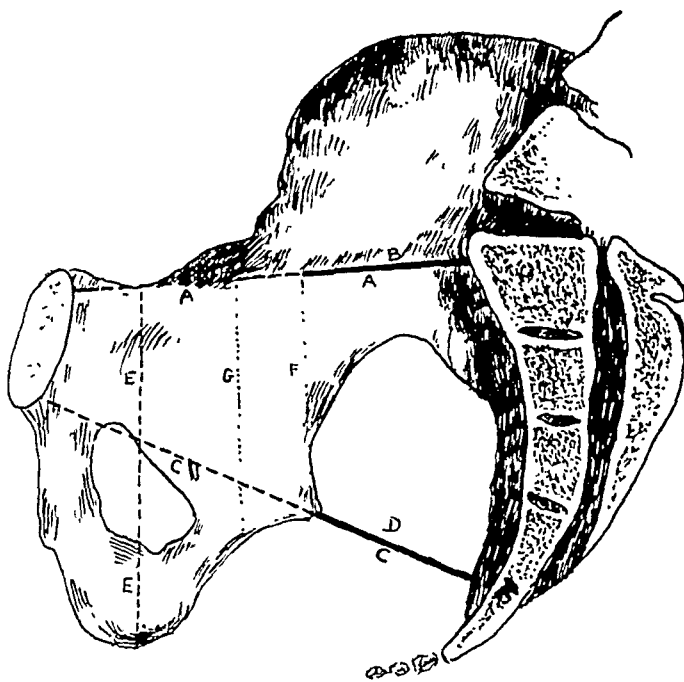


Fig. 2.—Lateral aspect of pelvis. *A*, Anteroposterior diameter of inlet; *B*, posterior sagittal diameter of inlet; *C*, anteroposterior diameter of midplane, *D*, posterior sagittal diameter of midplane.

According to the classification which we have found the most useful, these ranges are divided according to the following pelvic types: Dolichopellic, mesatipellic and brachypellic. The incidence of these pelvic types in a larger group (1,100 women) consecutively studied was 19, 46 and 32 per cent, respectively.

The present paper is concerned with the relative shortening of two midplane dimensions, the interspinous or transverse diameter and the anteroposterior diameter. Our interest in this relative shortening arises from the fact that, in our experience, dystocia at the pelvic midplane resulting from the shortening of these diameters is not uncommon and, when such shortening is present, a knowledge of its degree is of considerable prognostic value. When midplane contraction exists and the pelvic inlet diameters remain within average limits, the fetal head usually shows good engagement, labor proceeds in a natural manner but becomes difficult as the head attempts to pass the midpelvic plane. It is at this level of the pelvis, rather than at a lower point, as Hanson has pointed out, that the greatest difficulty in midforceps delivery is usually encountered.

In the present series of patients showing midplane contraction our particular interest has been in the incidence of operative delivery. It is proper, therefore, that we should consider the meaning of that term as here used. These women, 153 in number, were delivered upon the ward service of the hospital. The series represents delivery at term of 194 pregnancies—153 first and 41 subsequent pregnancies. The operative deliveries represent midforceps, low forceps and cesarean sections. In each case where operative intervention was used, a definite indication was present. In other words, no "prophylactic" or "elective" forceps were performed. In the very few breech cases which occurred, extraction was counted as spontaneous birth unless the forceps were also used in the delivery of the aftercoming head.

In the present study we have chosen to regard a midplane transverse diameter of 10.0 cm. as the lower limit of normal and have, therefore, chosen for this study 153 women whose pelvis showed midplane transverse diameters less than this figure. In this group the distribution of pelvic types was as follows:

| | |
|---------------|--------|
| Dolichopellic | 42.4 % |
| Mesatipellic | 41.1 % |
| Brachypellic | 15.6 % |
| Platypellic | 0.65% |

The high incidence of the first two types is to be expected, for relative narrowing of the pelvic sidewalls is characteristic of these types. For purposes of analysis, we have divided the series into two groups: Group A, in which the range of the midplane transverse diameter was 9.9 cm. to 9.6 cm. (65 instances); and Group B 9.5 cm. to 8.4 cm. (88 instances). When we consider that in the former group the operative

incidence at delivery was 37.1 per cent and in the latter it was 57.6 per cent, the reason for such division becomes obvious.

Some of the pelvises in this series also showed diminution at the pelvic inlet; in other words, were "small" pelvises according to a criterion² previously set down, which is:

| | |
|---------------|---|
| Dolichopellic | type showing an inlet anteroposterior of less than 12.0 cm. |
| Mesatipellic | type showing an inlet anteroposterior of less than 11.5 cm. |
| Brachypellic | type showing an inlet anteroposterior of less than 10.5 cm. |

Of the 153 women, 36 possessed pelvises which were accordingly "small," and these were distributed according to type:

| | |
|---------------|----|
| Dolichopellic | 7 |
| Mesatipellic | 24 |
| Brachypellic | 5 |

In all instances the contraction at the inlet was not enough to prevent the head from descending to the midplane during labor. The incidence of all operative procedures was 50 per cent and it may be that the influence of the inlet contraction, in addition to that of the midplane, shared the responsibility for such interference.

In discussing midplane pelvic contraction, both transverse and anteroposterior diameters must be considered. When both are relatively shortened, it seems apparent that dystocia must be considered as likely to occur. A knowledge of the average dimensions of the midplane anteroposterior diameter is, therefore, also of importance. In the previous study of 500 women, as shown in the table, these are as follows:

| | |
|--|-------------------|
| Dolichopellic anteroposterior midplane | 12.0 to 13.0 cm. |
| Mesatipellic anteroposterior midplane | 11.75 to 13.0 cm. |
| Brachypellic anteroposterior midplane | 11.5 to 12.75 cm. |

In the present series of 153 primiparous women, 75 showed that, in addition to midplane transverse contraction, anteroposterior shortening was also present. These were distributed according to pelvic type as follows:

| | |
|--------------------|----|
| Dolichopellic type | 27 |
| Mesatipellic type | 36 |
| Brachypellic type | 12 |

The operative incidence in both A and B groups was 54.6 per cent, but, if we consider those pelvises falling in Group B (transverse diameter 9.5 cm. or less), the operative interference rose to 65.0 per cent. In other words, definite transverse shortening plus anteroposterior shortening at this plane markedly increases the incidence of operative intervention. This high incidence is in contrast to 73 pelvises (vertex presentation) in which the transverse midplane contraction was not accompanied with anteroposterior shortening. Here the operative incidence was 41.3 per cent for the whole group, and for Group B, 45.2 per cent.

Thirty-two of the 153 women were subsequently delivered on our wards of their second pregnancies, eight of their third child and one

of her third and fourth. Sixteen of these women who were delivered spontaneously of their first infants were also delivered spontaneously in subsequent pregnancies. In the remaining 16 women in whom the first pregnancy was ended by operative intervention, 9 were subsequently delivered spontaneously. The remaining 7 were delivered in the second labor by operative means, but in each instance the midplane transverse was 9.2 cm. or less and in 4 there was present, in addition, definite anteroposterior shortening. Six of these women had pelves which were of the dolichopellic type. In the 9 cases delivered by operative means in the first labor but later spontaneously, all but two showed transverse midplane diameters greater than 9.2 cm. and midplane anteroposterior shortening was present in but four, and in these only to a slight degree. There was one dolichopellic pelvis in this group.

Summary of the Study

| | | | |
|--|-------|-------------------------------------|----------|
| Number of pelves studied | 153 | | |
| Number of labors | 153 | first, 32 second, 8 third, 1 fourth | |
| Pelves showing midplane transverse less than 10.0 cm. | 153 | instances | |
| Pelves showing midplane transverse 9.9 to 9.6 cm. | 65 | instances | |
| (Group A) | | | |
| Pelves showing midplane transverse 9.5 to 8.4 cm. | 88 | instances | |
| (Group B) | | | |
| Group A operative incidence | 37.1% | Low forceps | 16 times |
| | | Midforceps | 7 times |
| Group B operative incidence | 57.6% | Low forceps | 28 times |
| | | Midforceps | 18 times |
| | | Cesarean section | 3 times |
| Pelves showing relative midplane transverse shortening plus inlet anteroposterior shortening | 36 | instances | |
| Operative incidence in this group | 50.0% | | |
| Pelves showing midplane transverse shortening but no other shortening | 73 | instances | |
| Operative incidence | 41.3% | (Group B alone 45.2%) | |
| Pelves showing midplane transverse shortening plus midplane anteroposterior shortening | 75 | instances | |
| Operative incidence | 54.6% | (Group B alone 65.0%) | |
| Group A—32 cases | | Group B—43 cases | |
| Low forceps | 8 | Low forceps | 15 |
| Midforceps | 5 | Midforceps | 10 |
| | | Cesarean section | 3 |

In summarizing this experience we wish to observe that midplane pelvic contraction, as indicated by shortening of the transverse diameter, combined or not with shortening of the midplane anteroposterior diameter, is definitely associated with increased operative intervention

during labor. When the midplane transverse diameter is 9.5 cm. or less and the other diameters remain in average limits, according to this study the incidence of intervention was 45.2 per cent. When midplane anteroposterior shortening was also present, operative incidence was 65.0 per cent. In subsequent deliveries, midplane transverse shortening of 9.2 cm. or less with and without accompanying anteroposterior shortening also carries a high incidence of operative necessity. In the patients in this series who were not delivered by operative means, the incidence of prolonged labor in both first and second stages was of frequent occurrence.

Many obstetricians will agree that in certain instances elective cesarean section is to be preferred to the difficult midforceps operation with its frequent attendant severe trauma to both mother and child. It is hoped that by such studies as this, a clearer evaluation of midplane contraction may be secured, so that the conduct of labor may be based less on rule of thumb methods and more on those which offer factual knowledge.

In conclusion we wish to emphasize that, although the knowledge of essentially exact pelvic measurements should never replace sound clinical judgment, which obviously includes the evaluation of the size of the child, character of the labor, etc., the intelligent consideration of such knowledge should form an important aspect of scientific obstetrics.

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A STUDY OF THE ENDOMETRIAL PATTERN BEFORE AND AFTER TREATMENT FOR AMENORRHEA

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CESSATION of the menses during the reproductive years in the absence of pregnancy, castration, hysterectomy or a masculinizing tumor is a serious and common gynecologic complaint. Diligent study and intensive therapy are often necessary if the reproductive life of the woman is to be salvaged. This report records the observations made upon 9 women whose chief complaint was secondary amenorrhea. The term, secondary amenorrhea, as used in this paper means a cessation of the menses for a period of 5 months or more. A much larger number could be reported if the cases of 2, 3 and 4 months' amenorrhea were included but here the effects of therapy are more difficult to evaluate because of the probability of spontaneous menstruation.

Sex physiology has for its ultimate purpose the procreation of the species. The complex pituitary-ovarian-endometrial system, of which menstruation is but the terminal event, has for its purpose the cyclic maturation of a potentially fertile ovum and the preparation of the endometrium for nidation (Fig. 1). It is believed by many that menstruation per se serves no useful physiologic function. The presence or absence of ovulation is therefore all important physiologically. Accordingly, the 9 amenorrheic patients under consideration here have been divided into 2 groups on the basis of their microscopic endometrial patterns. This provides the best means for determining the presence or absence of ovulation. The finding of a persistent proliferative phase endometrium at successive weekly biopsies indicates a failure of ovulation and therefore a serious pituitary-ovarian defect.¹ The finding of a persistent secretory endometrium at successive biopsies suggests the influence of a persistent corpus luteum.² Differentiation of the amenorrheic patients into those with proliferative and those with secretory phase endometria is essential to correct therapy as will be evident later in this paper. Repeated endometrial biopsies at weekly intervals are necessary to establish the endometrial type. No patient was included in this group unless at least three biopsies taken at approximately weekly intervals were available for study.

Amenorrhea Associated With Proliferative Phase Endometrium

Seven of these 9 patients had a persistent proliferative phase (anovulatory) endometrium. These endometria varied from a very atrophic type with scarcely any glandular structure (Case 1—Fig. 2), to a marked hyperplasia such as that shown in Case 7 (Fig. 2). Examina-

tion of the endometriums from these 7 amenorrheic patients shows a wide variation of endometrial pattern in this type of amenorrhea. (Fig. 2.) The pattern in any one case, however, is extremely constant. When weekly biopsies were taken on these patients, it was found that there was an amazing persistence of the endometrial pattern in each individual patient. For this reason only one photomicrograph from each patient is shown, this being the biopsy taken just before beginning treatment. In each case this third biopsy was identical with the previous two on that patient.

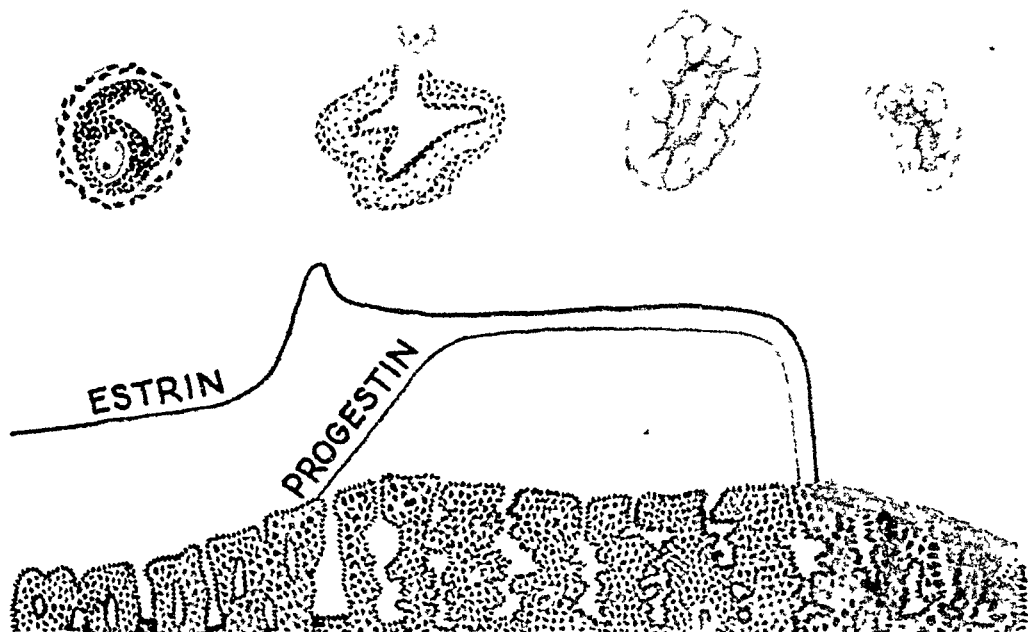


Fig. 1.—Under stimulation of the gonadotropic hormone from the anterior pituitary the Graafian follicle is stimulated to grow and after about two weeks of growth it ruptures extruding the ovum. Estrogen produced by the growing follicle shows the growth or proliferative phase in the endometrium. Under influence of the corpus luteum, the secretory phase of the endometrium is produced with its fuzzy, saw-toothed glands. Sudden atrophy of the corpus luteum about the 26th day of the cycle brings about a sudden estrogen-progesterone withdrawal which provides the bleeding stimulus to the spiral end-arteries of the endometrium.

The pathologic physiology involved in anovular amenorrhea is fairly well understood. It is thought to be the result of a pituitary-ovarian failure, primary or secondary to some systemic disease. Due to insufficient gonadotropic stimulation from the anterior pituitary or to refractivity of the ovary, a Graafian follicle fails to mature and there is no ovulation.¹ No rise and fall in the estrogen level occurs as one finds in the normal cycle; there is no progesterone and so the normal estrogen-progesterone withdrawal from the involuting corpus luteum is absent. (Fig. 1.) Thus, the usual stimulus to the spiral end-arteries of the endometrium is absent and no bleeding occurs. The persistent, unchanging pattern of the endometrium week after week indicates a fixation of the hormone level. Since bleeding usually follows sudden estrogen or progesterone withdrawal, the normal stimulus to menstruation is lacking.



Case 2.

Fig. 2.—Amenorrhea with proliferative phase endometrium.

Case 1.—First endometrium after 3 years' amenorrhea, marked atrophy of both the stroma and glandular structure. No change followed treatment. No menstruation. Patient's age, 19.

Case 2.—First endometrium taken from a patient, aged 26, after 11 months' amenorrhea. Note the atrophy of the glandular structure but fairly good stroma. Second biopsy taken at onset of bleeding episode 4 days after completing first course of treatment. No bleeding followed second course of treatment and no menses occurred afterward.

Treatment.—Since the normal stimulus to uterine bleeding is the sudden withdrawal of estrogen-progesterone from a higher level to a lower one (Fig. 1), an attempt was made to simulate this normal physiology and thus induce uterine bleeding.² After the patients had been adequately studied by successive biopsies, they were given stilbestrol 5.0 mg. daily at bedtime for 10 nights. On the last 5 days of the stilbestrol therapy, it was supplemented by progesterone 5.0 mg. daily intramuscularly.³ Following this intensive 10-day therapy, uterine bleeding occurred in 6 of the 7 patients within 4 days. The average duration of the induced menstruation was 3.5 days. One patient (Case 1), who had such marked atrophy of the endometrium, failed to menstruate. In the 6 successful patients, the 10-day course of treatment was repeated on the fifteenth day from the first day of the induced bleeding. Stilbestrol 5.0 mg. was given for 10 days supplemented by progesterone 5.0 mg. on the last 5 days of the 10-day treatment. In other words, the treatment was given from the fifteenth to the twenty-fifth day of the induced cycle. Five of the 6 patients had another episode of uterine bleeding within 15 days after completing the second course of therapy. No further treatment was given. Of the 5 patients in whom a second bleeding phase was induced, all continued to menstruate at fairly regular intervals for periods of 7, 3, 12, 9 and 12 months respectively without further treatment. Of these, 2 lapsed into their original amenorrheic state when treatment stopped, but only after 3 and 9 months of spontaneous menstruation respectively.

An endometrial biopsy was taken at the onset of the first induced menstruation in the 6 patients. Photomicrographs of these endometriums can be seen in Fig. 2 opposite the endometriums from the same patients prior to treatment. It will be noted that in no case was there a marked alteration in the endometrial pattern as a result of treatment. This lends further evidence to the belief that menstruation is a spiral end-artery phenomenon induced by estrogen-progesterone withdrawal having little relation to the endometrial pattern.

CASE 1.—Virgin, aged 19, had 3 scanty menses at the age of 16, amenorrhea for 3 years. She had an infantile uterus with marked atrophy of the endometrium. (Fig. 2.) No bleeding followed the course of treatment described above. Patient has been followed for 2 years and no menstruation has occurred. This amenorrhea may be the result of an endometrial defect not related to any endocrinopathology.

CASE 2.—M. L., aged 26, menses always regular, menarche at 17. Amenorrhea of 11 months when first seen. Endometrium moderately atrophic. Stilbestrol-progesterone treatment was followed by scanty menstruation on the fourth day. Second course of treatment followed by no bleeding episode. No menses since. (Fig. 2.)

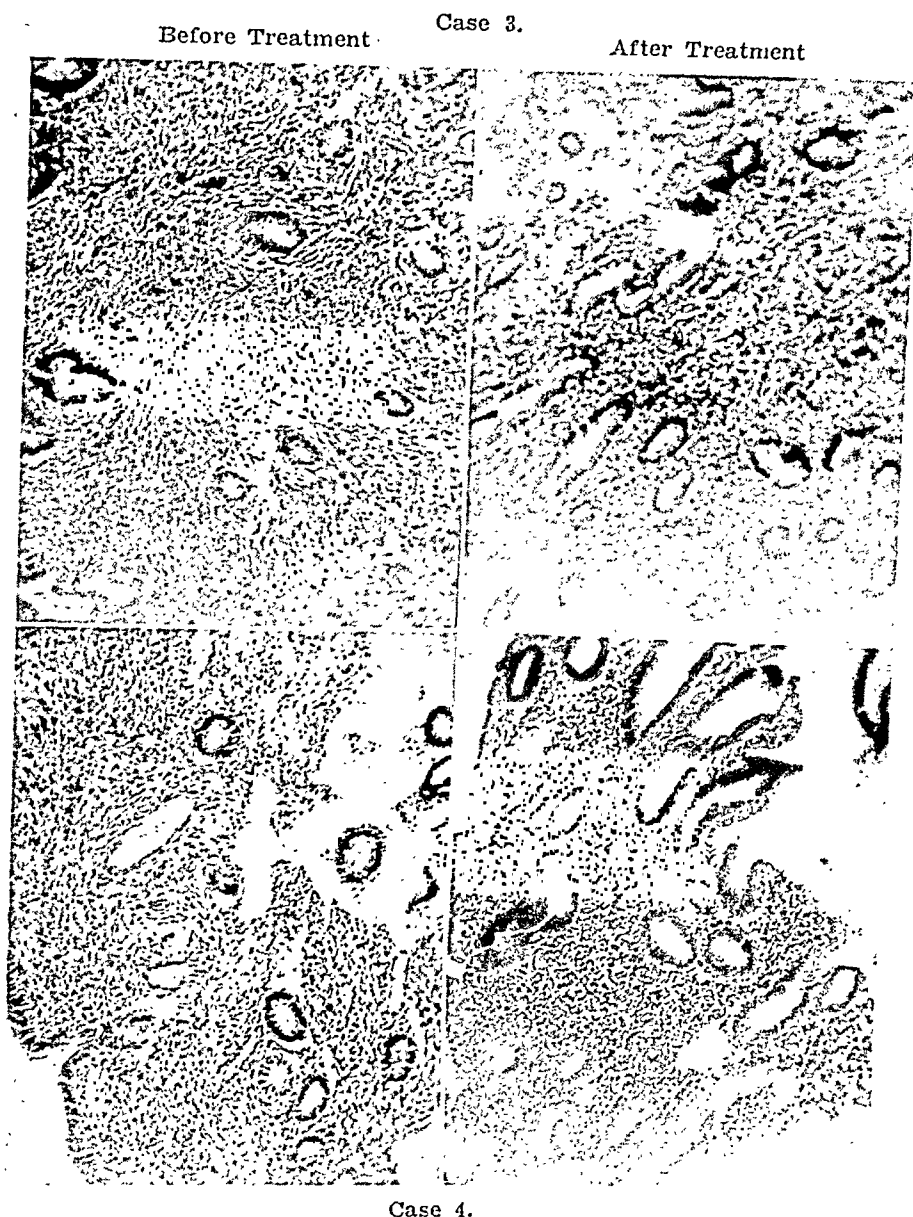


Fig. 2.—Amenorrhoea with proliferative phase endometrium.

Case 3.—First endometrium taken on patient, aged 22, after 5 months of amenorrhoea which began suddenly. Menstrual cycle had previously been regular. Second endometrium on this patient at onset of bleeding episode 4 days after completing first course of treatment. Cyclic menstruation recurred for 7 months and stopped.

Case 4.—First endometrium taken on a patient, aged 33, whose amenorrhoea dated from a difficult delivery complicated by hemorrhage 18 months previously. Second endometrium taken just before bleeding episode following treatment, note that despite the induction of bleeding, there is no demonstrable change in the endometrium. Two months of treatment was followed by cyclic menstruation for 3 months at which time the patient could no longer be traced.

CASE 3.—A. Q., aged 22, nulligravida, married, 3 years' sterility, menses fairly regular until last year, amenorrhea 5 months, persistent proliferative endometrium. Treatment was followed in 4 days by normal 6-day flow. Second course of treatment followed by normal flow and fairly regular menses persisted for 7 months without treatment and then stopped. (Fig. 2.)

CASE 4.—R. L., aged 33, para i, amenorrhea since delivery of still-born fetus as result of placenta previa 18 months previously. First and second course of treatment followed by normal menstruation which persisted for a period of 3 months at which time the patient disappeared. (Fig. 2.)

CASE 5.—M. C., aged 29, menses always irregular, menarche at 16, amenorrhea since spontaneous abortion with hemorrhage 7 months previously. Normal menstruation followed treatment and a cycle of 35 to 45 days has persisted for 1 year. (Fig. 2.)

CASE 6.—R. M., aged 23, normal menarche and normal menstrual cycle until 5 months previously. Menses stopped suddenly, amenorrhea since that time, persistent proliferative endometrium. Normal cyclic menstruation established following treatment described above and this persisted for 9 months without treatment (Fig. 2), at which time she lapsed into her amenorrheic state.

CASE 7.—L. S., aged 21, virgin, menses always irregular, amenorrhea for 5 months, persistent proliferative endometrium, polypoid. Normal cyclic menstruation has persisted for 1 year since treatment. (Fig. 2.)

Amenorrhea With Secretory Phase Endometrium

Two of the 9 amenorrheic patients here considered were found to have persistent secretory phase endometriums. (Fig. 3.) The presence of a secretory endometrium indicates a persistent corpus luteum. It has been shown by Corner and others that menstruation in the monkey may be delayed for long periods of time by the administration of large doses of progesterone. The presence of a persistent corpus luteum maintains the progesterone and estrogen level at a fixed point. Since no atrophy of the corpus luteum occurs, there is no estrogen-progesterone withdrawal and the normal stimulus to uterine bleeding is absent. This etiologic factor as a cause of amenorrhea is rarely diagnosed and these patients may go for many years sterile and without the psychic benefit of periodic menstruation.

CASE 8.—D. M., aged 27, nulligravida, menarche age 12, normal 28-day cycle until 14 months previously. Patient had her last menstrual period November, 1941. In January, she consulted an obstetrician who gave her prenatal care until April, 1942. At this time it was discovered that she was not pregnant and various types of chorionic gonadotropins

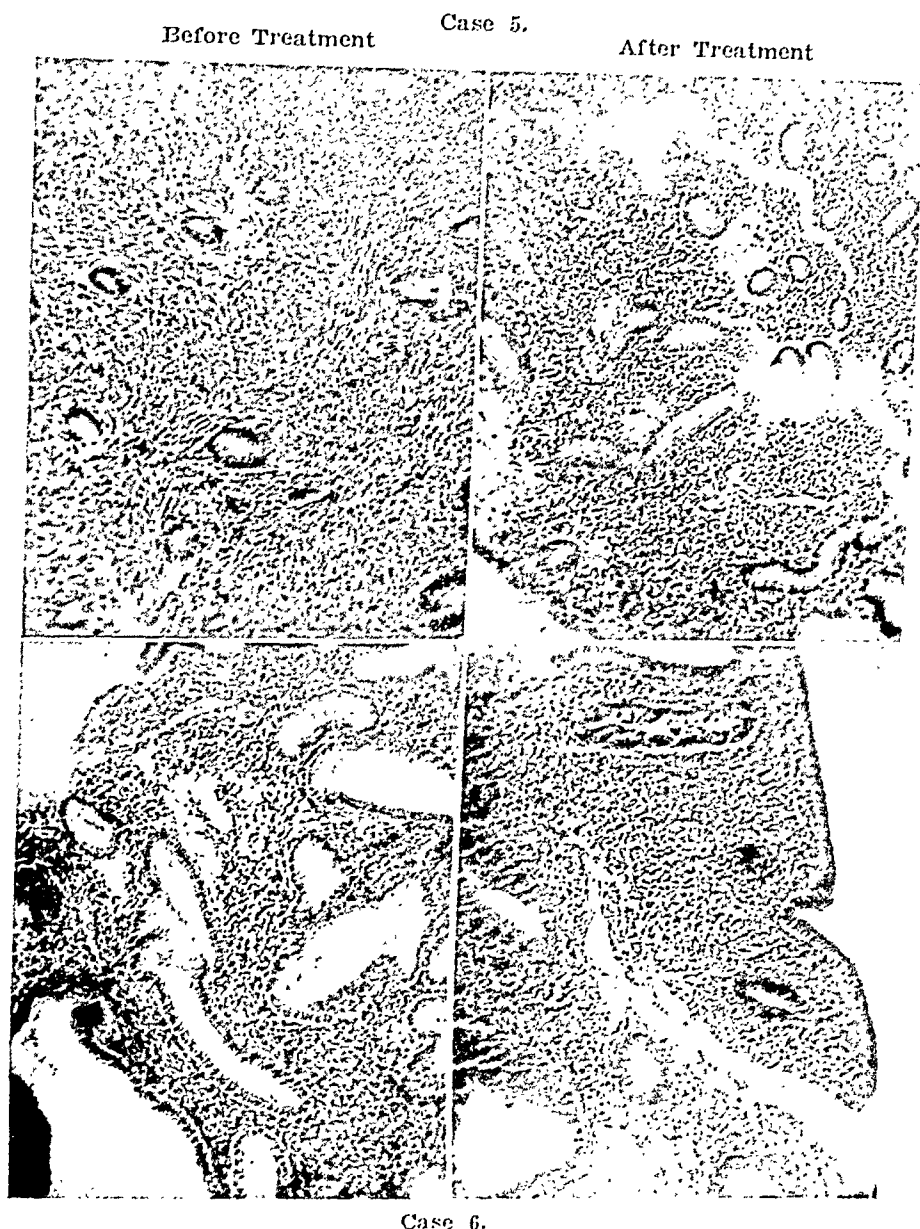


Fig. 2.—Amenorrhea with proliferative phase endometrium.

Case 5.—First endometrium taken on patient, aged 29, whose amenorrhea dated from an abortion with profuse hemorrhage 7 months previously. Normal proliferative phase endometrium. Following two courses of treatment, the endometrium shows some evidence of estrogen stimulation but no progestin influence. Despite little change in the endometrium, the patient had spontaneous but irregular menses which persisted for over a year after treatment.

Case 6.—First endometrium shows early cystic endometrium of a persistent proliferative phase. Taken on patient, aged 23, after 5 months' amenorrhea which occurred suddenly in what had previously been a regular cycle. Second endometrium shows no evidence of stimulation but menstruation followed treatment and has recurred at intervals of 28 to 30 days for 9 months.

were administered irregularly for a period of 6 months. She was seen in January, 1943, with no complaint other than amenorrhea of 14 months' duration. Endometrial biopsy showed persistent secretory phase. There was no pelvic pathology and the ovaries were normal to palpation. Despite a negative pelvis, the diagnosis of persistent corpus luteum was made and a laparotomy performed. At the operating table the ovaries were smooth and normal size, no follicle cysts. Incision deep into the right ovary exposed a healthy, glistening, yellow corpus luteum approximately 1 cm. in diameter. It was excised and menstruation followed on the second day and recurred at 27- to 31-day intervals until the patient became pregnant in August, 1943, after 6 years' sterility. (Fig. 3.)

Before Treatment

After Treatment

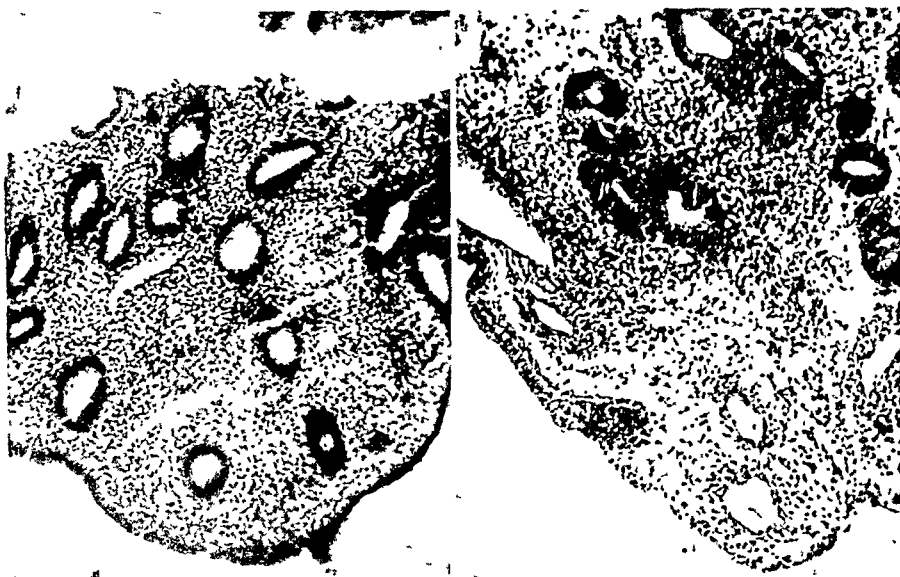


Fig. 2.—*Amenorrhea with proliferative phase endometrium.*

CASE 7.—First endometrium taken on patient, aged 21, menses always had been irregular but amenorrhea at the time of biopsy had persisted for 5 months. Polypoid proliferative phase endometrium. Following treatment the endometrium shows a cystic hyperplasia. Menstruation began the first 5 days after completing treatment and has recurred cyclically for over 1 year.

CASE 9.—V. C., aged 25, married 2 years with no pregnancies, came under treatment for sterility in September, 1942. Menstrual history always normal. Complete sterility study revealed anovulatory cyclic bleeding as the only sterility factor. No treatment was given but the patient failed to menstruate at the appointed time in December, 1942. She was examined by this author and thought to be pregnant. No symptoms of pregnancy and no weight gain prompted a re-examination in February, 1943. The uterus had not enlarged but the Friedman test was positive. The patient was followed for 2 more months during which time her amenorrhea persisted and the uterus did not enlarge. At this time, a soft, doughy mass in the region of the left ovary estimated to be 9 cm. in diameter could be palpated. Repeated endometrial biopsies



Case 9.

Fig. 3.—Amenorrhea with secretory phase endometrium.

Case 8.—Patient, aged 27, menses always regular until onset of amenorrhea 14 months previously. Repeated endometrial biopsies showed a persistent secretory phase such as that seen in the first photomicrograph. This was taken in the ninth month of amenorrhea, many different types of endocrine therapy had been used without success. Following removal of a persistent corpus luteum from the right ovary, menstruation occurred on the second postoperative day. Menstruation recurred at regular intervals and the next biopsy taken at the onset of the patient's third bleeding episode is shown.

Case 9.—Patient, aged 25, developed an amenorrhea of 5 months' duration, while under treatment for sterility. Friedman test was positive but patient was not pregnant. Repeated endometrial biopsies showed a persistent proliferative phase until onset of the amenorrhea when the endometrium assumed the pattern seen in the first photomicrograph. This was taken in the fourth month of amenorrhea. A corpus luteum cyst of the left ovary measuring 6 cm. in diameter was removed, menstruation followed in 3 days. The secretory endometrium seen in the first picture reverted to a normal proliferative one on the fourteenth postoperative day. Normal cyclic menstruation has persisted since that time. The absence of pregnancy was confirmed by curettage at the time of operation and no chorionic villi were found.

at this time revealed a persistent secretory phase endometrium. The patient was operated upon by the author in May, 1943. A corpus luteum cyst of the left ovary about 6 cm. in diameter was removed. Thorough curettage revealed no chorionic villi. (Fig. 3.) The patient menstruated on the third postoperative day and a normal cyclic menstruation has occurred since that time.

Summary

A comprehensive study on 9 patients with a history of amenorrhea persisting for 5 months or more is presented. Endometrial biopsies taken at weekly intervals made it possible to divide these patients into 2 classes as follows:

1. *Amenorrhea With Persistent Proliferative Phase Endometrium.*—Patients with this type of amenorrhea are usually true endocrine problems, their pathologic physiology being a pituitary-ovarian failure with absence of ovulation. The proliferative endometriums vary from the atrophic proliferative type to that of cystic hyperplasia. The endometrial pattern for each individual patient remains amazingly constant. This suggests that the estrogen level in these individuals is a fixed one and in the absence of any cyclic variation of this hormone level, the spiral end-arteries of the endometrium are denied their normal stimulus for bleeding. It is the estrogen-progesterone withdrawal which provides the end-artery stimulus in the normal woman. Satisfactory treatment for this type of amenorrhea is available in the form of stilbestrol 5.0 mg. daily for 10 days supplemented during the last 5 days with progesterone 5.0 mg. Uterine bleeding follows in 3 to 4 days in most cases and the course of treatment is repeated on the fifteenth to twenty-fifth day of this artificially induced cycle. Immediate results were good in that 6 of 7 patients menstruated immediately following treatment and 5 of them continued to menstruate without treatment for variable periods of time. An interesting observation is that despite the induction of bleeding, there occurred little change in the endometrial pattern following treatment. Comparison of the photomicrographs in Fig. 2 shows little difference before treatment and after menstruation had been induced.

2. *Amenorrhea With Persistent Secretory Phase Endometrium.*—A type of amenorrhea rarely diagnosed is that caused by a persistent corpus luteum. Two patients are reported with long periods of amenorrhea and on whom persistent secretory endometriums were obtained. Both patients were originally diagnosed as pregnant and, indeed, one was found to have a positive Friedman test. Both resumed normal menstrual cycles after excision of a small corpus luteum in the right ovary of one, and the removal of a corpus luteum cyst in the left ovary of the other after 14 and 6 months' amenorrhea respectively. Undoubtedly, there are some cases in which a persistent corpus luteum un-

dergoes atrophy spontaneously with re-establishment of the normal cycle. However, those patients with persistent amenorrhea in whom repeated secretory phase endometriums are obtained, a diagnosis of persistent corpus luteum or corpus luteum cyst can be made and the treatment is excision of the corpus luteum.

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GENITAL TUBERCULOSIS IN THE FEMALE

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THE low incidence of genital tuberculosis in the female seldom permits the accumulation of cases in number sufficient to be of significant statistical importance. Only by the continued reporting of smaller series can an adequate literature be built up, and to this end the present report is made. Recent articles^{9-11, 14-16} tend to give the impression that the disease commonly involves only one or two of the pelvic structures. This trend is undesirable, since it has been our experience that the disease is usually widespread, and therefore not readily amenable to limited therapeutic measures.

Material

Sixty-two cases seen between January, 1920, and July, 1941 form the basis for this report. In every instance the diagnosis was confirmed by histologic examination, a criterion of selection by which unproved cases are excluded.

The patients ranged in age from 15 to 61, the average being 30 years. Sixty per cent were between 20 and 40 when admitted.

The complaints which brought these patients to the hospital are recorded in Table I. It is evident that none is characteristic of the pelvic disease.

TABLE I. ADMITTANCE COMPLAINT

| COMPLAINT | NUMBER OF PATIENTS | PERCENTAGE |
|---------------------|--------------------|------------|
| Abdominal pain | 22 | 35.4 |
| Sinuses or fistulas | 10 | 16.0 |
| Vaginal bleeding | 7 | 11.3 |
| Back pain | 7 | 11.3 |
| No complaints | 3 | 4.8 |
| Ascites | 2 | 3.2 |
| Abdominal tumor | 2 | 3.2 |
| Amenorrhea | 2 | 3.2 |
| Other | 2 | 3.2 |
| Pruritus vulvae | 1 | 1.6 |
| Urinary symptoms | 1 | 1.6 |
| Sterility | 1 | 1.6 |
| Dysmenorrhea | 1 | 1.6 |
| No statement | 1 | 1.6 |
| | 62 | 99.6 |

Abdominal pain had led to operative intervention in 12 patients prior to their first admittance to the University of Michigan Hospital.

Since the endometrium and ovaries are commonly involved—as will be shown later—some change in the menses might be expected. This was the case in 58.1 per cent of the patients in this series (Table II).

While these menstrual changes cannot be considered characteristic, it is of interest to point out that hypermenorrhea and irregularity of

TABLE II. MENSTRUAL ABNORMALITIES

| TYPE | NUMBER OF PATIENTS | PERCENTAGE |
|-------------------------|--------------------|------------|
| Irregularity | 16 | 25.8 |
| Hypermenorrhea | 13 | 20.9 |
| Amenorrhea | 6 | 9.7 |
| Polymenorrhea | 6 | 9.7 |
| Oligomenorrhea | 2 | 3.2 |
| Postmenopausal bleeding | 1 | 1.6 |
| No change | 19 | 30.6 |
| No information | 7 | 11.3 |

the menses occurred much more commonly than did amenorrhea, which so frequently has been stressed in connection with pelvic tuberculosis. Table III shows the correlation between ovarian and extragenital tuberculosis in our amenorrheic patients.

TABLE III. RELATIONSHIP OF OVARIAN AND EXTRAGENITAL TUBERCULOSIS TO AMENORRHEA

| CASE NUMBER | AGE | OVARIAN TUBERCULOSIS | EXTRAGENITAL TUBERCULOSIS |
|-------------|-----|----------------------|---------------------------|
| 1 | 28 | 0 | Generalized |
| 2 | 19 | 0 | Generalized |
| 3 | 20 | 0 | ? pulmonary |
| 4 | 22 | ?* | ? pulmonary |
| 5 | 17 | + | None |
| 6 | 19 | ?* | Pulmonary |

*Ovaries not examined.

It was surprising to note that tuberculosis was present in the ovaries of only one of the four patients in whom the ovaries were examined, and conversely, extragenital tuberculosis was extensive in two of these patients and was probably present in another. One might suspect that the amenorrhea depended more on the character of extragenital tuberculosis than on ovarian involvement. If this supposition were true, a poorer prognosis might be expected in those patients with amenorrhea. However, in our series the survival figures for the amenorrheic cases were practically the same as for the entire series. The long survival of two amenorrheic patients in whom extragenital tuberculosis was absent or questionable (Cases 4 and 5) may have given an abnormally high survival for the group.

Sterility.—The relation between pelvic tuberculosis and sterility is difficult to evaluate. Infertility is said to occur in from 7 per cent to 85 per cent of these cases, being less common in those with myometrial involvement and almost constant when the tubes are affected. Lahmann and Schwartz,⁵ considering all types of genital tuberculosis give the incidence of sterility as 26 per cent. In our series there were 46 married patients in the childbearing age. Twenty of these had not been pregnant, making the incidence of "infertility" 43.5 per cent. The word "infertility" is used advisedly since no investigation was made as to other possible causes.

Tuberculosis Elsewhere in the Body.—It is of the utmost importance that tuberculous lesions in other organs and systems should be sought and investigated as to extent and activity, since Peterson showed that these factors play a vital role in determining the outcome of cases surgically treated. Concomitant pulmonary involvement has been reported in from 20 per cent (Lahmann and Schwartz)⁵ to 36 per cent (Wetterdall).

In our series 48 per cent had other active foci in addition to the genital lesion. Table 4 shows the organs involved as determined by clinical or postmortem examination.

TABLE IV. ACTIVE EXTRAPELVIC TUBERCULOSIS

| SITE | NUMBER OF PATIENTS | PERCENTAGE |
|--------------------------|--------------------|------------|
| Lungs | 25 | 40.3 |
| Abdominal organs | 10 | 16.1 |
| Sinus tracts | 4 | 6.4 |
| Abdominal lymph nodes | 3 | 4.8 |
| Bones and joints | 3 | 4.8 |
| Trachea, larynx, bronchi | 2 | 3.2 |
| Kidneys | 1 | 1.6 |
| Bladder | 1 | 1.6 |
| None found | 32 | 51.6 |

It is probable that a more thorough search might raise the incidence in these sites. That we are, in recent years searching more carefully may be indicated by the fact that in the first half of the twenty-year period 42 per cent of the patients were found to have extragenital tuberculosis, while in the latter half of the period other foci were noted in 55 per cent.

Analysis of Treatment

Non-Operative Treatment:

Eight patients in this series received nonoperative treatment. Four of this group had far-advanced generalized tuberculosis, and operation was not considered advisable. Management in these cases was purely symptomatic and all died an average of 3.6 months after admittance.

Three patients were treated by bed rest, adequate diet, ultraviolet light, etc., and 2 are alive and well after 10 and 9 years respectively. The third patient in this group died within 8 months after admittance.

One patient with a tuberculous cervix refused treatment, but is alive and denies symptoms, except for amenorrhea, after 20 years. She is now 40 years old.

In these nonoperated cases, the diagnosis was confirmed by examination of biopsy or autopsy material.

Operative Treatment:

Fifty-four patients were treated surgically, the abdominal cavity being opened in 49. The latter can be divided into 3 groups for better comparison of end results with respect to fistula formation and wound infection:

- A. Complete pelvic exenteration, with total hysterectomy and bilateral salpingo-oophorectomy. ----- 13 cases.
- B. As in (A) except that the cervix was not removed. -- 13 cases.
- C. All other operations, including vaginal hysterectomy, removal of cysts, posterior colpotomy, drainage of abscesses, etc. ----- 23 cases.

Table V shows the relationship between the type of operation and the frequency of fistulas and wound infections present at the time of discharge.

TABLE V. RELATIONSHIP BETWEEN TYPE OF OPERATION AND WOUND COMPLICATIONS

| | GROUP A | GROUP B | GROUP C |
|--|---------|---------|---------|
| Number of cases | 13 | 13 | 23 |
| Number of wound infections or fistulas | 1 | 4 | 7 |
| Percentage of cases with wound infection or fistulas | 7.7 | 30.7 | 30.4 |

The figures in Table V suggest that perhaps tissue which was not removed at operation had something to do with the wound complications, though the operation may have been incomplete for good technical reasons.

The total incidence of fistulas or wound infection was 24 per cent. This is in marked contrast to the 54 per cent incidence among patients who had been operated on prior to admittance here. Greenberg² reported that wound infection occurred in one-third of his 200 cases, and that fistulas resulted in 17 per cent of the drained cases, but in none of those closed without drainage. Lehmann and Schwartz state that 53.3 per cent of their cases developed fistulas. It is interesting to note that we have had only two wound complications since 1930, and none in the 10 patients operated since 1936, although the number of cases has remained quite constant from year to year.

Operative Mortality:

The primary operative mortality was 5.5 per cent. Two patients died on the fourth postoperative day, one of pulmonary embolism, and the other of peritonitis and intestinal obstruction. A third patient died on the nineteenth day of generalized tuberculosis.

Distribution of Pathology:

The incidence of involvement of the various pelvic structures among all the pathologic specimens examined is shown in Table VI.

TABLE VI. DISTRIBUTION OF TUBERCULOSIS IN ENTIRE SERIES

| SITE | NUMBER OF CASES SHOWING INVOLVEMENT | PERCENTAGE |
|-------------|--|------------|
| Tubes | 44 | 70.9 |
| Parametrium | 39 | 62.9 |
| Endometrium | 27 | 43.5 |
| Ovaries | 17 | 27.4 |
| Cervix | 7 | 11.1 |
| Myometrium | 3 | 4.8 |
| Vulva | 1 | 1.6 |
| Vagina | 0 | 0.0 |

Since all the genital organs were not available for examination in every case, this table does not represent the true incidence of involvement. There were 13 operative and 5 autopsy cases in which all the internal genitalia were removed and examined. The distribution of tuberculosis for this group is somewhat different, as shown in Table VII.

As would be expected, the incidence of involvement has risen in all the tissues in this group, but of special interest is the increased cervix involvement. Our findings tend to bear out Jameson's² statement "... there is no doubt that if the cervix were removed in every hysterectomy and submitted to histological examination, the incidence of cervical tuberculosis would be greatly increased ..." It is the practice of many

TABLE VII. ACTUAL DISTRIBUTION OF PELVIC TUBERCULOSIS

| ORGANS AND TISSUES | NUMBER OF CASES | PERCENTAGE |
|--------------------|-----------------|------------|
| Tubes | 17 | 94.4 |
| Parametrium | 12 | 66.6 |
| Endometrium | 11 | 61.1 |
| Ovaries | 7 | 38.8 |
| Cervix | 5 | 27.7 |
| Myometrium | 3 | 16.6 |

when removing the uterus to leave the cervix in situ unless it is obviously diseased. There are times when it is unwise to subject the patient to the added risk and time required for complete hysterectomy. However, in view of the frequency of cervical involvement, it would appear advisable to perform a total hysterectomy whenever possible.

Follow Up:

All 62 patients in this series have been carefully followed. Seventeen (25.8 per cent) are dead after an average of 2.3 years. Five died of causes related to pelvic tuberculosis or its extension. The remaining 12 died of causes other than pelvic, the most common being pulmonary and generalized tuberculosis.

Forty-five patients (74.2 per cent) are alive, an average of 10.5 years after their original admittance. Over half of these (57.7 per cent) claim good health. Wound sinuses persist in only 2 patients.

Discussion

It is interesting to note that so few patients gave evidence of tuberculosis elsewhere in the body. There are several possible explanations for this:

- A. Tuberculosis may have been present elsewhere, but not discovered.
- B. The portal of entry may have been the genital tract, and spread elsewhere may not have occurred. It has been shown by Jameson² and others, that in laboratory animals infection of the genitalia can be accomplished by this route. Jameson also cites two human cases in which the evidence strongly suggests that the infection was of the ascending type.
- C. The infection may have been hematogenous, and the genital organs the most fertile field for its development, while the primary focus remained silent and undetected.

This leads to consideration as to whether genital tuberculosis is primary or secondary. The literature contains many cases thought to represent primary or secondary tuberculosis. Such reports may have some academic interest, but from a practical standpoint, it is the character and extent of extragenital tuberculosis, and not merely its presence or absence which is important for proper management of the patient.

Since the patients treated surgically and those treated conservatively were not similar in respect to extent and severity of the disease, the better end results in the former group cannot be construed as an indication that operative treatment is always preferable. The difficulty in establishing the diagnosis without operation continues to make evalua-

tion of nonoperative treatment hazardous. However, it seems to be the general opinion^{2, 6, 12, 13} that a patient will do better if the diseased tissue is removed by radical operation. Furthermore, Jameson, in reviewing the literature, found a composite salvage rate of 73 per cent for radical operative procedures and 62 per cent for conservative operations. The data in Table V definitely suggest that, at least from the standpoint of wound healing and fistulas, once the abdomen is opened, all the genital organs, including the cervix, should be removed if possible. Tissue conservation does not seem justified.

Summary

1. Data are presented on 62 cases of proved genital tuberculosis admitted to the University of Michigan Hospital during the last 20 years, with follow-up studies on all cases.
2. There were no clinical signs or symptoms pathognomonic of pelvic tuberculosis.
3. Sixty per cent of the patients were in the childbearing age.
4. Forty-three and one-half per cent of the married patients had not conceived.
5. One-half of the patients (51.6 per cent) revealed no evidence of active extragenital tuberculosis.
6. When operative treatment is indicated, all the genital organs including the cervix, should be removed if possible, even though the latter appears normal grossly.
7. Wound complications (infection and fistulas) are much more common after incomplete operations.
8. Seventy-four per cent of the patients in this series are alive an average of 10.5 years after their first admittance.
9. Fifty-four per cent of the survivors claim good health, with no untoward symptoms.

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THE FREQUENCY OF ANOVULATORY MENSTRUATION AS DETERMINED BY ENDOMETRIAL BIOPSY

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CORNER in 1927 was the first to suggest that the anovulatory cycles which he had observed in monkeys might occur in human beings.¹ Earlier investigators had reported that anovulatory bleeding occurred in the monkey, but Corner was the first to have a controlled group of animals with menstrual histories. He found that out of twenty-seven cycles only seven were ovulatory.^{2, 3} Later Hartman showed that anovulatory cycles could occur in monkeys at any time in the midst of a series of ovulatory cycles;⁴ and Bartelmez,⁵ in a review in 1937 cited seventeen satisfactory human cases in which menstruation had occurred at the expected time without either ovary containing a corpus luteum which could be ascribed to the immediately preceding cycle. The endometria, as Corner showed, were nonsecretory in type when anovulatory bleeding occurred, and Robertson, Maddux, and Allen⁶ demonstrated that uterine bleeding occurred in castrated monkeys following the withdrawal of injections of female sex hormone.

Anovulatory bleeding may be expected to be most frequent at the menopause and at puberty, when corpora lutea seldom occur and the Graafian follicles persist. These phenomena are correlated with the relative sterility of these periods.⁷ The frequency of anovulatory menstruation has been variously estimated. Mazer and Ziserman⁸ reported that twenty out of forty-one sterile women showed anovulatory cycles, whereas Tietze⁹ found that only 7 per cent of his sterility patients showed anovulatory endometria. Lass and his co-workers¹⁰ reported that in forty-seven lactating women with previously regular menses, 106 (55 per cent) of 194 cycles were anovulatory. Morton and Hayden found only 7 anovulatory cycles in 142 menstrual periods of thirty-three normal, regular, young women.¹¹

In our work we desired to determine the frequency of anovulatory menstruation in a group of women with previously regular menstrual periods. For our patients we were able to secure 103 cooperative women from among the female population of the Kankakee State Hospital. All of these women were psychiatric patients; all had regular menstrual periods. Endometrial biopsies were taken in almost all cases twenty days or more following the last menstrual period. In no case was a biopsy taken when the patient had been menstruating longer than forty-

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eight hours. In a few instances we were compelled to take biopsies earlier than twenty days after the preceding period. However, in this latter group, when the microscopic examination of the specimen revealed a nonsecretory endometrium, it was discarded and the biopsy repeated at a later date in the same cycle, or in the next cycle. The biopsies were taken from as high in the uterus as possible, two specimens being taken from the anterior wall, and two from the posterior wall as advised by Kotz and Parker.¹⁴ All of our biopsy specimens were stained with hematoxylin and eosin. In doubtful cases Best's carmine stain for glycogen, and the thionin stain for mucin were used to elucidate the diagnosis.

In the microscopic interpretation of the specimens, the following criteria were used as indicative of the secretory phase:

1. The presence of secretion, glycogen and mucin, within the lumina of the glands; subnuclear vacuolation was not considered to be a sign of early secretion since it has been shown that this may occur in castrated monkeys under estrogen stimulation alone; however, the presence of glycogen in the rest of the cell was taken as a sign of progesterone stimulation;^{12, 13}
2. Characteristic tortuosity of the glands, although this was not present in all the specimens diagnosed as being in the secretory phase;
3. Stroma abundant, particularly in the compacta, with relatively large round cells containing a fairly abundant cytoplasm, and with increasing vascularity and edema.

Since it is likely that some of our biopsies did not include a section of the entire endometrium and were mainly compacta, we relied upon the first and third criteria mainly, although in practically every section of secretory endometrium there was some degree of tortuosity of the glands.

Results

We obtained 261 satisfactory biopsies from 103 women. The pertinent information regarding these patients with anovulation and the results of the microscopic examinations are found in Table I. It will be seen that there are 67 women from whom 3 endometrial biopsies each were obtained. Not all of these, however, are from consecutive periods, since at certain times a previously cooperative patient will refuse to submit to examination only to reverse her attitude completely at a later date. There are also 24 patients with 2 biopsies each, and 13 with 1 biopsy each.

Of the 261 specimens only 14 were found to be nonsecretory, giving a percentage of 5.36. (Although various degrees of endometrial development were noted, we have simply classified our findings as either secretory or nonsecretory.) These 14 anovulatory cycles occurred in 9 or 8.67 per cent of the patients. Two patients showed 3 successive nonsecretory endometria. There was 1 patient with 2 anovulatory cycles out of 3; and 6 patients, of whom 5 had 3 biopsies, and one 2 biopsies.

TABLE 1

| TOTAL NUMBER BIOPSIES ANOVULATORY ENDOMETRIA | | | TOTAL NUMBER PATIENTS PATIENTS WITH ANOVULATORY CYCLES | | | | | |
|---|--------|-----|---|--|------------------|---|--|---|
| INCIDENCE | | | INCIDENCE | | | | | |
| 261 14 5.36% | | | 103 9 8.67% | | | | | |
| DATA OF PATIENTS SHOWING ANOVULATORY CYCLES | | | | | | | | |
| PT. NO. | NAME | GR. | AGE | MENTAL DIAGNOSIS | MENSES | L. M. P. | BIOPSY DATE | MICROSCOPIC DIAG. |
| 9 | C., M. | ij | 40 | Dem. precoc hebephrenic type | 2d. C. | 1. 2/16/41 2. 2/17/41 3. 3/26/41 | 1. 2/11/41 2. 3/ 5/41 3. 3/27/41 | 1. Nonsecretory 2. Secretory 3. Secretory |
| 11 | C., M. | 0 | 25 | Without psychosis Mental deficiency | 4d. Mild D. | 1. 2/ 5/41 2. 3/ 3/41 3. 3/28/41 | 1. 3/ 3/41 2. 3/24/41 3. 4/21/41 | 1. Nonsecretory 2. Nonsecretory 3. Nonsecretory |
| 20 | F., N. | ij | 35 | Dem. precoc hebephrenic type | ? | 1. 2/16/41 2. 3/22/41 3. 4/16/41 | 1. 3/ 4/41 2. 4/14/41 3. 5/ 5/41 | 1. Secretory 2. Secretory 3. Nonsecretory |
| 22 | G., E. | 0 | 28 | Dem. precoc hebephrenic type | 7d. Neg. | 1. 12/16/41 2. 1/20/41 3. 2/26/41 | 1. 1/11/41 2. 2/25/41 3. 3/20/41 | 1. Secretory 2. Nonsecretory 3. Secretory |
| 38 | K., L. | ij | 40 | Dem. precoc catatonic type | 3d. Neg. | 1. 2/23/41 2. 2/23/41 3. 4/19/41 | 1. 2/25/41 2. 3/18/41 3. 4/21/41 | 1. Secretory 2. Secretory 3. Nonsecretory |
| 55 | S., G. | ij | 43 | Dem. precoc hebephrenic type | 5d. Scoliosis | 1. 1/15/41 2. 3/24/41 3. 4/16/41 | 1. 2/24/41 2. 4/14/41 3. 5/ 8/41 | 1. Nonsecretory 2. Secretory 3. Secretory |
| 57 | S., P. | ij | 36 | Dem. precoc hebephrenic type | 4d. Neg. | 1. 2/ 5/41 2. 3/ 1/41 3. 3/25/41 | 1. 2/25/41 2. 3/22/41 3. 4/14/41 | 1. Nonsecretory 2. Nonsecretory 3. Nonsecretory |
| 67 | W., P. | 0 | 46 | Dem. precoc hebephrenic type | 4-5d. | 1. 12/15/41 2. 2/12/41 3. 3/13/41 | 1. 1/11/41 2. 3/10/41 3. 4/ 4/41 | 1. Secretory 2. Nonsecretory 3. Nonsecretory |
| 77 | M., E. | 0 | 33 | Dem. precoc simple type | ? | 1. 3/17/41 2. 4/ 7/41 | 1. 4/ 7/41 2. 5/ 5/41 | 1. Secretory 2. Nonsecretory |

which each showed one anovulatory cycle. Of the 9 patients showing anovulatory cycles, 4 were nulliparous, and 5 had borne children. Three of the nullipara were under 40 years of age; 2 of the parous women were under 40 years; 1 nullipara and 3 parous women were past 40 years of age. (Table II.)

TABLE II. PATIENTS SHOWING ANOVULATORY CYCLES GROUPED ACCORDING TO AGE AND PARITY

| PARITY | UNDER 40 YEARS OF AGE | 40 YEARS OF AGE AND OLDER |
|-------------|--------------------------|------------------------------|
| Nulliparous | 3 | 1 |
| Parous | 2 | 3 |

The 2 patients with the 3 successive nonsecretory periods were below 40 years of age. The first was 25 years old, a nullipara with regular menses, and completely normal physically. Her mental diagnosis was "Psychosis With Mental Deficiency." The second patient was a 36-year-old para ij with regular menses, physically normal with the diagnosis of dementia praecox. The patient with 2 successive anovulatory periods was 46 years old and nulliparous, suffering from dementia praecox, and physically normal. The remaining 6 patients were all patients with dementia praecox with no physical findings. The first was 40 years of age, a para ij; the second, 35 years of age and also a para ij; the third was a 28-year-old nullipara; the fourth a 40-year-old para ij; the fifth a 43-year-old para ij; and the sixth patient was a 33-year-old nullipara.

From our results it does not appear that parity affects the incidence of anovulation to any significant extent in women who are menstruating regularly. (Table II.) Of 46 nulliparous women, there were 4 who showed one or more anovulatory cycles, giving an incidence of 8.7 per cent; there were 57 parous women, 5 of whom had anovulatory cycles giving an incidence of 8.77 per cent. (Table III.)

TABLE III. GENERAL INCIDENCE OF ANOVULATION ACCORDING TO PARITY

| PARITY | TOTAL | NUMBER WITH ANOVULATION | PER CENT |
|-------------|-------|----------------------------|----------|
| Nulliparous | 46 | 4 | 8.7 |
| Parous | 57 | 5 | 8.77 |

Age would seem to influence the frequency of anovulatory menstruation. Of 36 nulliparous women under 40 years of age, 3 had nonsecretory endometria resulting in an incidence of 8.3 per cent; 2 parous women under 40 years of age were found to have anovulatory cycles out of a group of 29, giving an incidence of 6.89 per cent; 10 per cent of the nulliparous patients and 10.7 per cent of the parous patients, over 40 years of age, had anovulatory cycles. (Tables IV and V.)

TABLE IV. INCIDENCE OF ANOVULATION IN NULLIPARA ACCORDING TO AGE

| AGE GROUP | TOTAL | NUMBER WITH ANOVULATION | PER CENT |
|---------------------------|-------|----------------------------|----------|
| Under 40 years of age | 36 | 3 | 8.3 |
| 40 years of age and older | 10 | 1 | 10.0 |

TABLE V. INCIDENCE OF ANOVULATION IN PAROUS WOMEN ACCORDING TO AGE

| AGE GROUP | TOTAL | NUMBER WITH ANOVULATION | PER CENT |
|---------------------------|-------|-------------------------|----------|
| Under 40 years of age | 29 | 2 | 6.89 |
| 40 years of age and older | 28 | 3 | 10.7 |

Comment

Our results show that anovulatory menstruation is relatively an infrequent occurrence in regularly menstruating women. In women whose menses are irregular, the frequency would probably be higher. Parity is apparently of little significance; but age is a factor, there being a definite increase in the percentage of anovulatory cycles in women past 40 years of age. If a larger group of women was studied, it might be possible to show a definite percentile increase of anovulatory bleeding in women past 40 years of age with each successive year of life until the menopause was completed. There is another factor which we must consider, namely, that our patients are all psychotic women. Of the 9 women who menstruated without ovulating, 8 were schizophrenics, and 1 was a psychotic with mental deficiency. It is well known that schizophrenic patients often cease menstruating for variable periods of time after arriving at an institution; and also that occasionally shock therapy will halt menses. It is also possible that other disturbances may be more frequent in schizophrenics than other types of patients. Without intending to imply any particular type of personality trend, we note, however, that our incidence of 14 anovulatory cycles in 261 menstrual periods compares quite closely with Morton and Hayden's incidence of 7 anovulatory cycles in 142 menstrual periods occurring in 33 normal, regular, young women. Our incidence is 5.36 per cent; theirs is 4.9 per cent. It would have been most interesting to see the effect of gonadotropic hormone upon the endometria of the patients with successive anovulatory cycles, but we were not in the position to carry out this work.

Summary

1. Two hundred and sixty-one endometrial biopsies were taken the last one-third of the menstrual cycle from 103 patients in a mental hospital.
2. Fourteen anovulatory cycles were found in 9 patients. Two patients showed successive anovulatory cycles; seven patients showed both anovulatory and ovulatory cycles.
3. Parity was not found to be a factor, but women past 40 years of age were seen to show a higher incidence of anovulatory menstruation—7.69 per cent as compared to 10.52 per cent.
4. In this group of patients the incidence of anovulatory cycles was 5.36 per cent. The patient incidence was 8.7 per cent.

5. While all the women in this group are psychotic patients, the incidence of anovulatory menstruation in them compares quite closely with that found in normal, healthy women.

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ANALGESIA AND ANESTHESIA FOR OBSTETRICS, INHALATION METHODS*

W. ALLEN CONROY, CAPT., M.C., A. U. S., CHICAGO, ILL.

THE problems of pain relief in labor by inhalation methods have been obscured many times by the emphasis usually placed on actual drugs and apparatus. It would seem more fruitful to consider what distresses and disturbances that delivery causes mother and fetus, and what degree of narcosis will decrease or eliminate these undesirable phases of an otherwise physiologic process. With these in mind, one could then marshal drugs, methods and skills to reach the desired effects.

The average primipara of these civilized days is unfortunately encouraged in her fear of an unknown experience, by the careless use of the word "pains" by her friends, mother and doctor. She does experience "labor" in its simplest meaning, but unlike her primitive sister, her work is attended by varying degrees of real pain. This distress must not be confused with the underlying contractions of the uterus. Means are in existence to eliminate the pain without markedly affecting the uterine contractions, just as pain in any muscle may be alleviated by drugs, and without loss of consciousness.

The first step, then will be to divorce her from the fallacious and harmful idea that she must be relieved of either consciousness or memory of the birth process in order to undergo it in any degree of comfort. Not till she understands that there can be consciousness and memory of labor without distress, will we eliminate some of the hazards of overuse of drugs. Too much narcosis, whether from nonvolatile or volatile agents, leads to fetal respiratory embarrassment, and to weakening of the uterine contractions. We may use *light hypnosis* with nonvolatile drugs like the barbiturates, scopolamine and paraldehyde. In quite moderate dosage, these induce a state of mental relaxation which enables us to gain the apprehensive mother's confidence. We must, if possible, convince her that freedom from pain is obtainable while she consciously assists in the "work" that her uterus does. Even where we later fail to achieve analgesia, we may help her tolerate some pain if she has the knowledge that possible harm to her baby is being avoided. The term analgesia is literally used here, not as an improper substitute for the word amnesia. A patient who is in a deep sleep, and is aroused to wild activity by pain cannot be said to be freed of pain. To call this effect analgesia is misleading to ourselves, because safe doses of barbiturates and similar drugs are not analgesic, that is, they do not eliminate pain.

*Read at a meeting of the Chicago Gynecological Society, Oct. 15, 1913.

Having obtained the mother's confidence before her labor contractions have acquired any element of intolerable pain, we must next watch for the degree and character of what true pain does accompany the individual contractions as their amplitude increases. During the first stage and early second stage, the tolerance to pain may be greater than normal, due to the light hypnosis already mentioned, and some will be willing to fortify it by small doses of opiates. If the pain factor increases rapidly in severity, we must turn quickly to safer methods before confidence in us is lost.

It is excellent practice to observe the rapidity of onset, severity, and duration of the pain factor of each contraction, as soon as labor becomes painful enough to require stronger measures. (See Fig. 1.) A hand on the uterus, and the sound of the patient's breathing and her outcries will tell us quickly whether pain comes early or late in the contraction, how severe it is, and how persistent. Since for each subject, the pain element will usually parallel the nature of the uterine contraction, it suffices to make a mental graph of contraction alone.

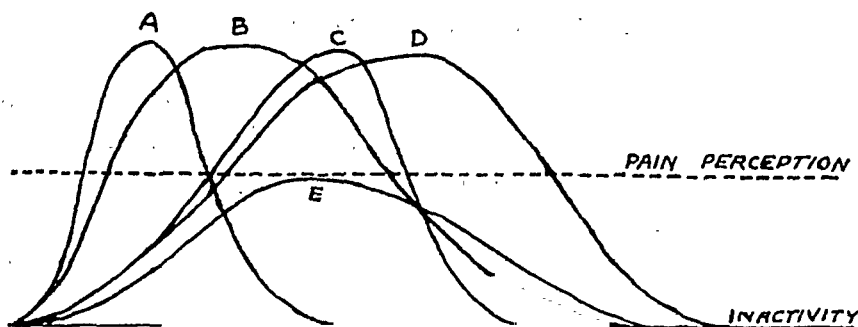


Fig. 1.—Types of contraction pain. A, Early, brief perception of pain; B, early, prolonged perception of pain; C, late, brief pain perception; D, late, prolonged pain perception; E, pain-free contraction.

Regardless of the inhalation agent used, the principle is the same. We must counteract the pain as rapidly as it builds up, without serious interference to the uterine contraction or hazard to the fetus. If the mother experiences severe pain almost simultaneously with the onset of the contraction, our efforts must be vigorous and swift. If the pain appears late, we content ourselves with the administration of oxygen till pain does appear. If pain is severe or persistent, we are taxed to provide enough pain relief to keep the mother from panicky ineffectuality.

For obstetrical analgesia, nitrous oxide remains our best weapon. Even the tyro will obtain fair results, and with safety, if the color of the patient is kept reasonably pink for the comparatively short time of each contraction, and if overoxygenation is achieved immediately after each contraction. Nitrous oxide may give the desired results with as low a concentration as 50 per cent where the pain element is minor, and may be used in its pure form for the brief and violently

painful contractions occasionally seen. (The lungs and tissues do have a small oxygen reserve.) When commencing to use nitrous oxide, it is wise to give it liberally, even to complete anesthesia, during one or two contractions, to fortify the patient's confidence in our ability to spare her distress. Using our mental graph of the character of pain, we then modify the gas mixture for each subsequent contraction.

If the peak of pain is reached early, the mother is instructed not to delay in asking for the gas, the instant she feels the uterus begin to contract. Better still, if the anesthetist is closely observing the abdomen manually, the first hardening of the uterus is a warning to start administration immediately. With the breathing bag already full with 70 per cent to 100 per cent nitrous oxide, and the valves and gas flow arranged so that all of each expiration is spilled into the outside air, the face piece is applied and the patient instructed to take two maximal inhalations as quickly as she is able. This gives a rapid displacement of the inert nitrogen from the lungs and achieves an analgesic level of the nitrous oxide before the contraction reaches its peak. As the second breath is being taken, the woman is instructed to hold that breath, and strain as if at stool. She will do this effectively once she is confident such activity will be relatively painless. If we know from previous observation that the contraction is short-lived, the breathing bag may be flushed now with pure oxygen. If it is going to be prolongedly painful, the gas is reduced to a level of 85 per cent or less, so that subsequent inhalations will be carrying in adequate oxygen.

Where the onset of pain perception is preceded by a period of painless contraction, three or even four rapid, full breaths of 70 per cent to 90 per cent nitrous oxide will be effective and safe. The longer time will allow for more complete flushing out of the inert nitrogen, but over such a period, the oxygen reserves would be depleted, hence the need for its addition to the gas. Subsequent gas flows for the expulsion efforts to follow will be adjusted to the anesthetist's mental picture of the curve of pain being experienced.

In all cases, flushing with pure oxygen for several breaths, as the uterus relaxes, is essential, to fortify both the mother's and fetus' tissues for the next contraction, when placental oxygen exchange will be reduced by the narrowing of the uterine sinuses and compression of the cord.

In addition to observation of maternal color, it is wise to have a means for the anesthetist to observe constantly any slowing of the fetal heart rate. A heavy stethoscope bell to be taped over the site of fetal heart sounds, and having tubing long enough to reach to the head of the delivery table has been described¹ for such a purpose. Slowing of the fetal heart, regardless of cause and time, should be the signal to increase the mother's oxygen intake immediately.

The other gaseous anesthetics may be, and are, used in a similar fashion. However, nitrous oxide is pleasant and noninflammable, while

ethylene has an unpleasant odor that may lead to nausea, and is inflammable. Its potency is only slightly more than that of nitrous oxide, so little is gained in oxygenation. Cyclopropane offers possibilities of unlimited oxygenation, and is pleasant, but it too is inflammable, and its very potency makes it easy to "overshoot the mark," producing a diminution in uterine contractions.

Of the volatile liquids, ethyl ether is most commonly used, but all too often either ineffectually or to the point of actual anesthesia, with reduction of uterine contractions. The safety factor is great, and its slowness to take effect may be no drawback where the pain of contraction is slow in developing to intolerable levels. Where pain is explosive, it is almost useless, unless a state of near-anesthesia is maintained constantly. Used this way, an increase in nausea, operative interference and fetal apnea is to be expected. Fetal apnea is rare with nitrous oxide alone, nausea is uncommon, and operative interference minimal.

Chloroform and vinyl ether come closest to duplicating the action of nitrous oxide, but the hazards of their use are many and well known. Liver damage is the most feared, but cardiac effects are more frequent and probably quite as dangerous. Other inhalation agents have not received adequate trial as yet.

When there is need for further analgesia or full anesthesia at the moment of expulsion or extraction of the fetus, nitrous oxide-oxygen alone is usually inadequate. Thorough procaine infiltration of the perineum, or the addition of small amounts of ether to the breathing bag are the safest supplementation.

Summary

The obliteration of the pain element of labor contractions is readily accomplished without loss of the patient's cooperation, and without interference with the strength of contractions, or danger to the fetus. Nitrous oxide, combined with oxygen inhalations and supplemented during expulsion, has been found adequate and safe in the hands of many. It, and the apparatus for its administration are available almost universally now, and personnel who know its use are much more plentiful than for the more complicated procedures frequently advocated.*

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*Papers by Drs. Buxbaum, Fitzgerald, Thomson and Brown, and Mengert follow.

Discussion on Symposium on Obstetrical Anesthesia on the Papers by Drs. Fitzgerald, Mengert, Buxbaum, and Conroy

DR. RALPH A. REIS, MODERATOR

DR. REIS.—What about the second twenty-four hours?

DR. MENGERT.—So far we have not had the courage to do it.

DR. REIS.—I would like to ask Dr. Windle a question with relation to what Dr. Conroy said about the time of cutting the cord.

DR. WINDLE.—We published some papers on that subject in which we made clear the reason for delaying until the placenta descended into the vagina.

DR. REIS.—Do you feel the increase in blood volume makes up for the added asphyxia?

DR. WINDLE.—I do not believe that there is additional asphyxia under normal conditions.

DR. CONROY.—During the time that the infant is lying outside the mother, the placenta still intact and the cord pulsating, it may be useful to increase the oxygen in the infant *via* the mother. If separation has occurred the cord should be cut.

DR. BROWN.—Would you add carbon dioxide to the oxygen?

DR. CONROY.—I feel, that the infant while in the mother, has a physiologic level of carbon dioxide from the mother's blood. It is the lack of oxygen that is going to kill it. If you are moving oxygen in and out of the baby's lungs you will keep the baby alive until its sensitivity to normal stimuli occurs. I will not say I have any objection to the use of carbon dioxide, but I feel in most instances, it is not needed.

DR. WINDLE.—I would like to say a word because a year or two ago I spoke to this Society on the use of carbon dioxide in some experimental animals. I am heartily in accord with what Dr. Conroy has just said. It is an academic question, whether you should use carbon dioxide in oxygen or not up to a certain point. The main thing is to get oxygen into the baby when he needs it. If the nervous system and respiratory center of the baby are depressed by barbiturates and other drugs and if the infant's carbon dioxide level is already very high, only then would the use of carbon dioxide with oxygen be contraindicated.

DR. REIS.—Dr. Mengert, have you ever used caudal anesthetic for cesarean section?

DR. MENGERT.—About four times and it has worked very satisfactorily.

QUESTION: Was it continuous or a single injection?

DR. MENGERT.—Continuous.

DR. REIS.—What is your opinion Dr. Huber?

DR. CARL HUBER, Indianapolis, Ind.—We have been using caudal anesthesia in Indianapolis since 1940. We have accumulated about 100 cases of delivery through the birth canal with caudal with results very comparable to those described. In that group, we did not notice the blood pressure drop that Dr. Mengert mentioned as occurring quite frequently. After this experience, we tried caudal anesthesia for cesarean section. The first patient on whom we tried caudal had had two previous sections, the first because of eclampsia, the second one because of the previous section. We followed her completely through the prenatal period in her third pregnancy. She showed no evidence of hypertension, the highest blood pressure being 130/80, with no albumin or other evidence of toxemia. She was given caudal anesthesia with 1.5 per cent metycaine. The injection was preceded by barbiturates. After she had a total injection of 30 c.c. of 1.5 per

cent metycaine, given first as 8 c.c., then 22 c.c., she went into vasomotor collapse, the blood pressure dropping to around 60/40 and staying at that level for a period of approximately three-quarters of an hour in spite of the administration of ephedrine, hypertonic glucose solution and finally plasma. While the blood pressure was at that low level, the fetal heart dropped to 60 beats per minute. When her blood pressure came back to a normal level after this three-quarters of an hour interval, the fetal heart rate returned rapidly to its previous level. We postponed section for 24 hours and it was then performed under general anesthesia. The baby was delivered and breathed without difficulty. It proved, however, not to be a normal baby. The infant was hospitalized for six weeks. It had a few convulsive movements, was stuporous all the time and required gavage feeding. It is now seven months old and is very definitely an abnormal baby. We have no proof, but it is our opinion that this collapse under the caudal anesthesia caused the damage.

We did not feel that this one case should represent the total of our experience, so we tried it again and it worked well. The third section in which we tried caudal anesthesia was in a patient who had had one previous section. She had had a normal prenatal course and it was an elective section at term. We began the caudal anesthesia according to the same technique. About ten minutes after the second injection, for a total of 30 c.c. of 1.5 per cent metycaine, she also went into collapse which was less severe and less prolonged than our first case. She, too, responded to ephedrine. The fetal heart tones dropped to around 50 to 60 per minute and stayed at that level for a period of 15 minutes. We went ahead with the caudal when she responded and injected more metycaine without further reaction and continued the cesarean section. The baby made one or two respiratory efforts and then we were unable to resuscitate it.

We, of course, cannot be sure whether or not the caudal anesthesia was the predisposing factor in these two disastrous instances. They have made us very cautious in the use of caudal anesthesia for section. We wonder if there might be something different in the response of the vascular system in a patient who is not having uterine contractions, and if the danger of vasomotor collapse is not greater than in a patient in active labor. We have done in all five sections, the two described being disastrous as far as the babies were concerned. I would like to ask Dr. Mengert if he has noticed any effect on the fetal heart rate in cases where the mother's blood pressure drops.

DR. MENGERT.—It was a mistake for me to say all four of our sections were done under continuous caudal. One case was an elective cesarean section, in which the patient received 50 c.c. of 2 per cent metycaine. We had no difficulty with the mother or baby in our four sections. The first was an especially interesting one because it occurred in an older patient with a diagonal conjugate of 10.5 Gm. and a disproportion which ordinarily would not be considered insurmountable. The patient was given caudal anesthesia and the resident actually attempted to do a high forceps, but had the good judgment to desist. After two hours of second stage with the membranes ruptured and attempted forceps, a successful section was done. That is why we feel that caudal anesthesia is contraindicated if there is any degree of dystocia which might ordinarily be overcome.

DR. REIS.—In Dr. Huber's case do you think there was any connection between the condition of the infant and the caudal anesthesia?

DR. WINDLE.—I do not think so.

DR. FITZGERALD.—We have done sections under caudal anesthesia and we have not had that particular experience.

DR. BROWN.—We have done eight or nine sections at the Cook County Hospital and in several we did have a fall in blood pressure, but without harm to the

mother or baby. In one case, we had an unusual type of anesthesia to the level of the clavicle, but without any drop in blood pressure or symptoms of respiratory distress.

DR. REIS.—Dr. Brown, will you tell us something about pontocaine *versus* procaine. Do you consider 10 injections in one patient safe?

DR. BROWN.—I think that is carrying things pretty far. That was one reason we sought a longer acting drug than procaine or metycaine. The frequency of injections depends largely on the type of drug, and whether or not epinephrine is employed. Dr. Mengert mentioned using 30 c.c. of 1.5 procaine every 30 to 45 minutes, which involved giving from 400 to 600 mg. of procaine per hour. That is a lot of procaine for the liver to detoxify.

By selecting the drug called pontocaine (Winthrop's brand of U.S.P. tetracaine), we are employing an agent with ten times the potency, and at least double the duration of procaine. On an absolute dosage basis, pontocaine is more toxic than procaine, but when allowance is made for the even greater increase in potency, Nowak found that in cats pontocaine had a corrected toxicity ratio 42 per cent lower than procaine. Is this ratio of 0.58 for pontocaine compared to 1.0 for procaine applicable to the human? Perhaps not, but our clinical experience with pontocaine in spinal and other regional nerve blocks suggests that it is. It conforms to the experience of James of England who uses pontocaine for extensive nerve blocks and infiltration. He regularly obtained three hours of abdominal anesthesia with no toxic effects. We are obtaining three to five hours of anesthesia with our initial dose of pontocaine (1:1,000) in caudal anesthesia. Subsequent injections average a shorter duration, but usually longer than one hour. I would estimate that caudal anesthesia is maintained in pontocaine cases by our technique at the Cook County Hospital with 8 to 20 mg. per hour. Even after multiplying these figures by 10 to convert to the equivalent dosage of procaine, it is evident we are introducing much less drug into the patient than the 400 to 600 mg. per hour of procaine required in Dr. Mengert's technique. The local anesthetic must be absorbed into the circulation and transported to the liver for detoxification. By reducing the total amount of drug, as well as by using a clinically less toxic agent, we feel we are reducing the incidence of toxic systemic reactions. As reported by Dr. Fitzgerald, we have had no major circulatory or respiratory complications. The minor symptoms such as transient headache, precordial distress, and aching in the legs, are phenomena coincidental with, and we feel associated with too forceful an injection of the solution. The major safety factor of any caudal technique should depend on a careful aspiration test, followed by the routine use of a slowly injected test-dose so calculated that it would be a safe intraspinal dose should the needle have penetrated a low-lying subarachnoid space.

We agree with Dr. Buxbaum on the importance of adding a vasoconstrictor to the anesthetic solution as an added safety factor. The addition of suprarenin (1:1,000) in amounts to make a concentration of 1:200,000, contributes definitely to prolongation of the anesthesia from each dose, and makes effective the low (1:1,000) concentration of pontocaine. Without the vasoconstrictor, a higher concentration and more frequent injections would be necessary and, systemic absorption being more rapid, toxic effects would be more likely. Ninety-nine of our 200 cases were performed with pontocaine 0.10 per cent (1:1,000) with suprarenin 1:200,000 (2 minims of 1:1,000 to the ounce) dissolved in physiologic saline.

We agree that continuous caudal anesthesia is limited in its usefulness, effectiveness, and safety, chiefly by the time, skill, and experience of the administrator. Our experience has been that a physician can learn the basic fundamentals of technique in a week, but that a month of training involving 20 or 30 personal administrations affords a more ample competence. No physician should

attempt continuous caudal anesthesia without previous practical experience under expert supervision. Only by adhering to this dictum will this new technique avoid the disrepute that will follow failures and complications, in inexperienced hands.

We should point out while Dr. Huber is here, that he modestly refrained from mentioning that Manalan, of his clinic in Indianapolis, preceded all others historically in the development of a technique for insertion of a ureteral catheter in the caudal canal (early in 1940). In our series at Cook County Hospital, we employed the Hingson safety caudal needle in 90 per cent of the cases, but our use of the 15 gauge Irving needle for introduction of a No. 4 French Bard caudal catheter, confined to 10 per cent of the first 200 cases, will increase in the future.

DR. CONROY.—I think it will be recognized by any one who has done a lot of caudal injections that we are injecting a drug into a highly vascular area and if this is done rapidly, it will bring about circulatory depression. It has been our practice to give a prophylactic vasoconstrictor, like neosynephrine, and when collapse occurs to administer oxygen as well as stimulants to diminish the anoxemia to both mother and baby.

DR. REIS.—Is there not work being done on anesthetic agents with more prolonged action which will not require keeping the needle in place?

DR. CONROY.—Some work is being done at the present time which will give analgesia for five to six hours. The idea was to enable the operator to give a single injection and repeat it perhaps not more than once, using ordinary stock needles which are easier to insert than are the complicated needles.

DR. ALBERT H. LAHMANN, Milwaukee, Wis.—I cannot understand why there are likely to be toxic reactions in caudal anesthesia in cesarean sections. We have reported 58 consecutive sections done under single injection caudal without any toxic reactions and without any additional anesthesia required during the operation. One possible factor is that these patients must be premedicated. Our routine is to give the patient about two hours before the scheduled section $4\frac{1}{2}$ grains of seconal or nembutal, then we inject approximately 75 c.c. of 2 per cent metycaine. Thus far, we have had no untoward reactions. It is true, we may have had a fall in blood pressure which is very transitory. We may have slowing of the fetal heart tones for a short time, but it has never worried us. The thing that has impressed us most is that these babies cry immediately when born. The loss of blood is minimal and the patient goes back to her room in excellent post-operative condition. She takes fluids immediately and is a very cooperative patient.

In 1939 at the County Hospital, Milwaukee, we started work on single injection caudal. In 1942, Dr. Mietus and I reported in *Surgery, Gynecology and Obstetrics* (74: 63-68) (Jan.) 450 cases. Since that time, we have given 800 single injections, 78 for multiparas and 722 for primiparas. Complete failure occurred in 4.5 per cent. Failure is due either to technical difficulty in getting into the canal, or sometimes to inability to get anesthesia even when in the canal. Partial anesthesia occurred in 6.7 per cent. This gives a total of 11.2 per cent failure and 88.8 per cent complete success.

Out of the last 450 caudals done at the County Hospital, there were five stillbirths. In breaking this down, one finds that the fetal heart was absent before the injection in 1; prolapse of the cord occurred in 1; an anencephalic monster was found in 1; the fourth was a premature weighing 3 pounds 9 ounces; the fifth was a case of abruptio placentae.

The duration of the anesthesia averaged about one hour and 29 minutes. The quantity of anesthetic in a single injection was about 45 c.c. We occasionally found a drop in blood pressure, which was transitory, and sometimes a little disorientation, but in review, we found that those patients who had disorientation were those patients in whom the barbiturate had not had a chance to take effect.

In these 800 cases we have no local infections. We do not use a wheal because we feel that it obscures the landmarks. I would rather give the patient a whiff of gas for a few minutes while we are inserting the needle.

We have in Wisconsin a new organization called the Wisconsin Society of Obstetricians and Gynecologists, which met this year. The entire meeting was devoted to a practical discussion of what was the status of caudal anesthesia. A committee was appointed to publish a statement in the *State Journal* and then be given to the lay press, telling the public what the obstetricians in the state of Wisconsin thought about continuous caudal. This has been completed. After Dr. Lundy spoke in Milwaukee last Friday and after the committee meeting with Dr. Cunningham of Columbia Hospital, we have gone on record as condemning continuous caudal as a procedure in private practice. Dr. Mengert and Dr. Fitzgerald are working in teaching institutions which are not suffering from loss of man power and nursing care as we are. It is impossible to get away from complications in continuous caudal anesthesia in private practice. Nevertheless, this committee went on record as saying that single injection caudal anesthesia in obstetrics has merit in selected cases. I am sure that three-fourths of the cesarean sections done in the city of Milwaukee are done under single injection caudal. In selected cases, particularly persistent occiput posteriors, breech extractions and perineal floor repairs where a little relaxation is helpful, single injection caudal is a success and I certainly think we are all going to continue to use it in cesarean section.

DR. REIS.—

Dr. Mengert, would you like to comment on single injection caudal?

DR. MENGERT.—We have had no experience with single injection caudal, so I am not competent to comment on it. We used it a few times some years ago and gave it up because it was too cumbersome a procedure to use for routine delivery, and the same result could be obtained with pudendal block. It was not until the continuous method appeared that we revived our interest in caudal anesthesia.

LOCAL ANESTHESIA*

HENRY BUXBAUM, M.D., CHICAGO, ILL.

(From the Chicago Maternity Center)

USUALLY, when one gets up before a critical audience such as this and presents his views relative to a certain type of obstetric analgesia or anesthesia, he almost automatically is placed in a position of attempting to defend his particular method. Fortunately, I was delegated by our moderator to present the case of local anesthesia. I say fortunately, because local anesthesia needs no defense, inasmuch as infiltration as well as regional anesthesia provides anesthesia to the part that is to be operated on rather than to the organism as a whole. Also I respectfully call to your attention that local anesthesia has all the advantages of the other types of anesthesia without any of their disadvantages.

Regarding the margin of safety in the various forms of anesthesia, as a general rule it can be said that the safety of any anesthetic agent increases in direct proportion to the distance with which it is administered from the brain and/or the central nervous system. With this fact in mind, I believe safety of the various forms of anesthesia can be stated in the following sequence:

1. Local infiltration, which is the farthest from the brain.
2. Regional or nerve block, such as parasacral or presacral, and pudendal.
3. Epidural or caudal.
4. Spinal.
5. General or inhalation anesthesia.

The advantages resulting from the employment of regional and local anesthesia are as follows:

1. No anesthetic mortality.
2. No pulmonary complications. Most obstetric patients come to the delivery room with full stomachs, making it almost impossible for even the best anesthetist to give her a smooth anesthetic. Excessive emesis, laryngospasm and aspiration pneumonia are not at all uncommon.
3. Simplicity of administration.
4. No paralytic ileus.
5. No fetal asphyxia.
6. Patient is able to take fluids by mouth during and immediately following the operation.
7. Less local blood loss due to adrenalin.
8. Less tissue trauma with better healing of the wound.

*Presented at a meeting of the Chicago Gynecological Society, October 15, 1943.

9. No interference with the efficiency of the uterine contractions.
10. Perineal floor relaxation with vaginal gaping, and finally, -
11. Less postoperative shock.

Among the few disadvantages may be cited:

1. In highly emotional patients, total success with local anesthesia may be impossible and therefore a general anesthetic may have to be supplemented.

2. All surgeons are not temperamentally adapted to use this form of anesthesia, due to a lack of patience, which is a prime requisite for the successful use of local anesthesia, and to the marked tendency toward rapid surgery, which is not at all necessary or even desirable in regional or infiltration anesthesia. Also, every surgeon using local anesthesia must have a wholesome respect for tissue integrity.

3. A minor disadvantage is the accidental breakage of the needle in the tissues, which can be obviated to a great extent by using a long needle and not inserting it up to the hilt.

Regarding the indications for local anesthesia. It has been satisfactorily demonstrated that all major and minor obstetric procedures either by the abdominal or perineal routes can be done under local anesthesia with the possible exception of version. An absolute indication for the use of local anesthesia may be found in patients with upper respiratory infections, pulmonary tuberculosis, asthma and cardiac disease with the omission of the adrenalin. Relative indications are pre-eclamptic toxemia, nephritic toxemia and diabetes. It is also the ideal approach in all cesarean sections with or without sterilization. Here one may use intravenous anesthesia in addition for closure if necessary. In the delivery of a breech presentation, parasacral or pudendal block is especially efficacious due to the relaxation of the pelvic floor and levators. Even if the operator should elect to use inhalation anesthesia, delivery is definitely facilitated by the addition of pudendal block.

Preparation.—According to deTakats, when distilled water is used as a vehicle for a 0.5 or 1 per cent novocain solution, the solution becomes slightly hypotonic, which has a tendency to hemolyze red blood cells and to produce tissue necrosis. Heating of stock solutions also diminish its anesthetic properties. Therefore, we always prepare our anesthetic in normal saline solution just prior to its use. Three minims of adrenalin (1:1,000) are added for each ounce of solution.

Technique.—As a precautionary measure in parasacral or pudendal block anesthesia, one should aspirate before injecting so as to make certain that the point of the needle is not in a blood vessel. In the infiltration method, the solution is deposited in the tissues with the needle in constant motion.

In the infiltration method, the posterior fourchette, lower posterior portion of the vaginal tube, and the ischiorectal fossae are injected. If an episiotomy is to be done, the line of incision is also injected.

In pudendal block, bilateral intradermal wheals are made midway between the tuberosity of the ischium and the anus. Then a 10 to

12 c.c. long, 20 gauge needle is directed to the spine of the ischium with a finger in the vagina or rectum to act as a guide. The point of the needle impinges against the spine, is then disengaged and passed to the dorsal aspect of the spine. Here, 10 to 15 c.c. of the solution are injected, effectively blocking the internal pudic nerve as it passes through the greater sciatic notch immediately posterior to the inferior ischial spine. Then the needle is withdrawn and a shorter needle is substituted, and 5 to 10 c.c. are deposited medial to the inner aspect of the tuberosity of the ischium in a fan-shaped manner, blocking the posterior femoris cutaneous nerve, a branch of the posterior fibers arising from the first and second sacral nerves. This same procedure is repeated on the opposite side.

In the parasacral or presacral technique, a finger is placed in the rectum and the sacrococcygeal joint is palpated. An intradermal wheal is made 2 c.c. from the midline at the level of the sacrococcygeal junction. A 15 c.c., 20 gauge needle is inserted parallel to the midline. The point of the needle feels its way over the edge of the last sacral vertebra and then advances 5 to 7 c.c. until the second sacral foramen is encountered. Then aspirate, and if no blood is drawn, inject 60 to 70 c.c. as the needle is being withdrawn. The angle of the needle is then shifted 15 degrees upward and again advanced parallel to the midline about 10 c.c. until the first sacral foramen is reached. Here, 20 to 30 c.c. of the solution are deposited. This process is now repeated on the opposite side. Lastly, 10 c.c. of the novocain solution are injected between the sacral coccygeal joint and the posterior wall of the rectum, blocking off the anococcygeal plexus.

Regarding the use of local anesthesia in abdominal deliveries, some men elect to use this method routinely, while there are other operators who only resort to local anesthesia when definitely indicated by the physical condition of the mother. Be that as it may, while the percentage of failures is greater in abdominal deliveries than in perineal deliveries, it is by far the safest form of anesthesia we have today at our disposal. The mother usually leaves the table in excellent condition, and is quite elated after hearing her child's first lusty cry. The babies are not lethargic or asphyxiated as they usually are when an inhalation anesthetic is used, but on the contrary cry immediately on their exit from the uterus.

The infiltration method is the most commonly used form of local anesthesia in cesarean sections, although one can block the nerves at the semilunar line if he so desires. Usually the method described by De Lee, and recently modified by Beck, is the method of choice of most obstetric surgeons. Here the three main sites for the deposition of the novocain solution are the skin and subcutaneous tissues, laterally in a semicircle from within, outward to a depth of about 5 c.c. before opening the fascia, and lastly under the loosely attached visceral peritoneum covering the lower uterine segment.

To demonstrate the practicability and safety of regional and infiltration anesthesia, let me briefly cite the statistics of the operative and spontaneous deliveries done at the Chicago Maternity Center with this method of anesthesia. Here, as you are aware, all deliveries are done

in the home under the poorest of physical and sanitary environments. These cases were nearly all done by our resident physicians under the supervision of the attending obstetricians. Up to the present time, from the inception of the institution in 1932, parasacral anesthesia has been utilized in 550 cases, and pudendal block in 2,200 cases, with no maternal or fetal deaths attributable to the anesthetic. There were two cases of abscess formation at the site of puncture. No needle was broken off in the tissues.

If we accept Farr's description of an ideal or successful anesthesia as one in which the operative procedure was completed with no pain or discomfort to the patient, a satisfactory anesthesia as one in which the indicated procedure was completed with only a slight amount of discomfort, and a failure as a case where the local anesthesia had to be abandoned or supplemented with inhalation anesthesia, then our results can be classified as follows:

In the 550 cases where parasacral anesthesia was employed, 314 (57 per cent) were ideal; 203 (37 per cent) were satisfactory; and only 33 (6 per cent) were failures.

In the pudendal block group, 880 cases (40 per cent) were ideal; 1,210 (55 per cent) were satisfactory; and 110 (5 per cent) were failures.

In the parasacral series, all forms of pelvic obstetric surgery were performed with the exception of version. This includes manual and instrumental rotations and difficult midforceps operations. In those cases in which the pudendal block anesthesia was used, the operations were mainly low forceps deliveries, episiotomies and repairs. This was also the procedure in all breech deliveries.

In closing, I wish to submit the following suggestion: Inasmuch as local anesthesia has proved so satisfactory in home obstetrics, it certainly can and should be employed more often in hospital practice, particularly in this day and age, where the anesthetic departments in most hospitals have been so badly depleted.*

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*See Discussion on Symposium on Obstetrical Anesthesia, page 85.

CONTINUOUS CAUDAL ANESTHESIA WITH PONTOCAINE: OBSTETRICIAN'S VIEWPOINT*

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CONTINUOUS caudal anesthesia as suggested by Hingson and Edwards¹ for women in labor has been used by many investigators in all parts of the country. Many reports have been published, but both the profession and the public are still far from clear concerning the indications for use of the procedure, or the disadvantages and even dangers associated therewith.

The following report is a preliminary presentation based on the first 200 cases in which repeated caudal injections of pontocaine were used to produce and maintain anesthesia during labor, and covers the five-month period between March 16 and August 26, 1943.

It may be well to note that we speak of *anesthesia* during labor, for this is more than analgesia, for in successful cases the patient, after the introduction of the needle, proceeds through her labor without even the slightest discomfort or awareness of her uterine contractions. It is the only pain relief yet devised that allows a parturient to smile through the hardest uterine contraction and mean it. Nevertheless, certain factors make the obstetrician somewhat cautious in his adoption of the procedure. It is the purpose of this report to present the obstetrician's reaction to the method insofar as the comfort and safety of mother and child are concerned.

Technique

Inspection of the sacral landmarks, an enema, and a soap and water cleansing of the skin over the sacrococcygeal region are preliminary steps. In this series a modified knee-chest position was used in most cases, as this insures accurate identification of the midline. The technique of identification of landmarks, insertion of needle, and evaluation of criteria for accuracy of placement, will not be considered in this paper. Though recommended, a barbiturate was rarely given for premedication. The solutions employed were made up as outlined in Table I:

Technical precautions designed to prevent complications include (1) limitation of concentration, amount, and frequency of injections to the least effective values which will produce and maintain relief of pain; (2) use of a vasoconstrictor in the anesthetic solution; (3) careful aspiration tests; (4) preliminary injection of a safe spinal test-dose con-

*Presented at the Oct. 15, 1943, meeting of the Chicago Gynecological Society. Credit is given to Dr. Bernice Rosen, M.D., and Miss Sedonia Spinka for assistance in the initiation and conduct of this series. Winthrop Chemical Company, Inc., supplied the Pontocaine 250 mg. ampoules and Suprarenin which were used in this series.

TABLE I. PONTOCAINE-SUPRARENIN SOLUTIONS

| CONCENTRATION OF PONTOCAINE | PONTOCAINE HCl "NIPHANOID" | SUPRARENIN* 1:1,000 | PHYSIOLOGIC SALINE |
|-----------------------------|-------------------------------|------------------------|-----------------------|
| 0.10% (1:1,000) | 250 mg. | 1.25 c.c. | qs. 250 c.c. |
| 0.15% (1: 666) | 250 mg. | 0.83 c.c. | qs. 167 c.c. |
| 0.20% (1: 500) | 250 mg. | 0.63 c.c. | qs. 125 c.c. |
| 0.25% (1: 400) | 250 mg. | 0.50 c.c. | qs. 100 c.c. |

*To make 1:200,000 Suprarenin.

Experience in this series indicates that the 0.10% (1:1,000) pontocaine solution is most satisfactory, and since it is the safest concentration of the four listed, the higher concentrations were rarely used after the first 100 cases. This concentration was used in nearly one-half (99) of all the cases, as listed in Table II.

taining 5 to 10 mg. of pontocaine followed by a delay of 10 minutes; (5) *slow* injection of therapeutic doses; (6) availability of an oxygen machine, a barbiturate, and a 15 gauge spinal puncture needle; (7) rigid asepsis; (8) preference of ureteral catheter technique in cases likely to be prolonged. All patients are kept on their sides most of the time to prevent post-partum backache and needle breakage. One nurse can be taught to care for several caudal patients simultaneously. The Block-Rothstein² gravity drip test with saline is employed to identify location of the needle tip when doubt exists. The Irving³ 15 gauge special B-D caudal needle, preceded by the 18 gauge 5½ inch Irving "inner guide" needle,* has been used in 20 cases of the 200 for introduction of the No. 4 French Bard nylon boilable caudal catheter.† In other cases the Hingson B-D "safety caudal" needle or its predecessor was employed. Other technical details and the reasons for selection of pontocaine will be reported elsewhere.

Distribution of the two hundred cases studied, according to the average duration and total dosage with various dilutions of pontocaine, both with and without suprarenin as vasoconstrictor, are given in Table II.

TABLE II

| CASES | % PONTO- CAINE IN SALINE | HOURS UNDER CAUDAL | | | | DOSES | | AVERAGE AMOUNT IN C.C. |
|---------------------------|--------------------------------|--------------------|------|---------|------|-----------|-----------|------------------------------|
| WITHOUT SUPRARENIN | | | | | | | | |
| | | MAXIMUM | | AVERAGE | | MAXIMUM | AVERAGE | |
| | | HR. | MIN. | HR. | MIN. | NO. DOSES | NO. DOSES | |
| 20 | 0.25% | 27 | 30 | 5 | 32 | 15 | 3.41 | 80.6 |
| 11 | 0.20% | 10 | 25 | 5 | 35 | 7 | 4.0 | 85.5 |
| 5 | 0.15% | 12 | 55 | 8 | 23 | 9 | 4.8 | 132.2 |
| WITH SUPRARENIN 1:200,000 | | | | | | | | |
| 1 | 0.25% | 1 | | 1 | | 1 | 1.0 | 37.0 |
| 31 | 0.20% | 17 | 30 | 4 | 33 | 5 | 2.5 | 53.0 |
| 20 | 0.15% | 37 | 15 | 6 | 25 | 14 | 3.2 | 79.5 |
| 13 | 0.125% | 44 | 30 | 8 | 45 | 19 | 4.2 | 114.5 |
| 99 | 0.10% | 38 | 15 | 6 | 10 | 15 | 3.0 | 74.8 |

Several observers have reported a marked decrease in the period of cervical dilatation. This has not been our experience. In Table III is recorded the elapsed time from administration of the anesthesia to

*Irving catheter introducing needles were supplied by Becton-Dickinson Co., Rutherford, N. J.

†No. 328 caudal catheters were supplied by C. R. Bard, Inc., 79 Madison Avenue, New York, N. Y.

complete dilatation. While such figures are not accurate because rectal examinations are subject to error, nevertheless it is still apparent that in our series cervical dilatation is not accelerated. The further fact that 6 cases without disproportion resulted in prolonged labors (over 24 hours) suggests that the rate of cervical dilatation is not affected.

TABLE III. TIME REQUIRED TO COMPLETE CERVICAL DILATATION

| | PRIMIPARAS | | | | | | |
|-------------------|------------|--------|--------|--------|--------|--------|--------|
| | 3 cm. | 4 cm. | 5 cm. | 6 cm. | 7 cm. | 8 cm. | 9 cm. |
| Hours and Minutes | 9' 5" | 8' 27" | 6' 19" | 8' 10" | 3' 58" | 3' 14" | 1' 19" |
| No. of Cases | 7 | 19 | 21 | 13 | 20 | 22 | 13 |
| | MULTIPARAS | | | | | | |
| | 3 cm. | 4 cm. | 5 cm. | 6 cm. | 7 cm. | 8 cm. | 9 cm. |
| Hours and Minutes | 8' 45" | 5' 49" | 4' 4" | 2' 18" | 2' | 1' 6" | 1' 50" |
| No. of Cases | 9 | 16 | 15 | 12 | 5 | 5 | 2 |

Caudal anesthesia results in a complete paralysis of the perineal muscles. These patients cannot empty their bladders. They have no sensation at all when the head is on the perineal floor. They have no abdominal sensation from a level usually just below the umbilicus. Consequently, they have no stimulus to force the fetal head over the perineum. It is true that a proportion of such patients can be taught to use their abdominal muscles so that spontaneous delivery can be accomplished. Nevertheless, the incidence of instrumental deliveries (Table IV) is sharply increased particularly on a service which has used a minimum of analgesics.

TABLE IV

| | |
|--|-------------------|
| Incidence of forceps delivery 1939 | 12.84% (of 4,552) |
| Incidence of forceps delivery with caudal anesthesia | 70.5% (of 200) |
| Primigravidas | 83.6% |
| Multiparas | 42.5% |
| There were 3 breech deliveries | |

Disadvantages

We wish to remind you of an earlier statement that, when continuous caudal anesthesia is successfully established, the patient goes through labor without any discomfort whatsoever. Nevertheless, there are some unpleasant and occasionally dangerous factors in the use of this method which require consideration.

Care must be taken to prevent liquid skin antiseptic running down onto the vulva, where it will burn severely. The knee-chest position is uncomfortable to maintain for long, especially during contractions. The lateral, or modified Sims' position, is satisfactory for the experienced operator, and for patients with excellent landmarks. It should be employed in cardiac patients, and in those having such frequent and hard pains as to make them uncooperative in any other position.

The insertion of the caudal needle is frequently rather painful, though this is reduced by the skillful operator by careful infiltration of

the skin, subcutaneous tissue, and deeper layers adjacent to the periosteum and sacrococcygeal membrane using the same pontocaine solution made up for the caudal. The use of a smaller gauge two inch "finder" needle, through which 4 or 5 c.c. of solution are injected into the tip of the caudal canal when it first penetrates the membrane, decreases the discomfort of the larger following needle. More care to insure an adequate local tissue anesthesia is necessary when the large (15 gauge) catheter-introducing needle is to be employed, as it takes considerable force to introduce it into the caudal canal.

In this series most of the anesthetics were initiated by Dr. Brown, the Director of Anesthesia, or by one of three residents in obstetrics assigned to him for instruction in caudal techniques. A fair proportion of cases, however, was performed by "postgraduate physicians" who come for supervised practical experience in the method. Due to the exigencies of teaching and the difficulties encountered in the early experience of new personnel, the average time recorded in more than half the cases from the skin wheal to the test-dose was 19.6 minutes. This can be reduced to limits of 3 to 10 minutes by the more experienced operator on uncomplicated subjects. The time required to establish accurate insertion has been as much as 40 minutes in some cases. This period may be one of considerable discomfort to some patients. The opinions of the obstetrician and the anesthetist may differ as to the importance and severity of discomfort associated with insertion of the caudal needle or catheter, but in the last analysis, it is the patient who will tell you whether it was worth it, after the dramatic relief of all labor pain is effected.

Among other disadvantages are the potential major complications of circulatory or respiratory depression due to massive intraspinal injection, intravascular injection, unusually high extension in the peridural space, or systemic toxicity due to absorption. By good fortune and rigid adherence to the strict regime of precautions outlined, no such major complication has occurred. It is possible that the selection of pontocaine and the use of a vasoconstrictor (suprarenin) have influenced this favorable experience.

Another practical disadvantage is the time and attention of the administrator required for successful conduct of the method. Although many details of management can be entrusted to a nurse especially trained to this task, the patient must be followed more closely by rectal examinations by the intern or resident, and the anesthetist responsible for the case or one equally competent in judgment and technical facility must be available within the building or on 10-minute call. Frequent problems arise in the management of a caudal case that require experienced appraisal, judgment, and decision, to insure uninterrupted maintenance of relief. It has been the experience of all in our acquaintance who have given a considerable number of continu-

ous caudal anesthetics that as soon as they get far away from the patient something "goes wrong." One must stay within fairly close reach of the nurse supervising the cases to insure their complete success.

Results

One hundred seventy-one cases (85½ per cent) were classified as completely satisfactory. There were only 3 definite failures due to inability to locate the caudal canal. In 10 patients there was initially complete relief, but later the needle became dislodged (5 cases) and was not or could not (1 case) be reinserted, or the needle was removed too soon, or the tubing became disconnected, or the catheter became plugged, resulting in return of pain, all 10 being classified as "technical interruptions" of the method. Six patients had incomplete relief in two of whom anesthesia was unilateral only. In 9 other cases of incomplete anesthesia, the deficiency *was* remedied by technical corrections such as addition of the vasoconstrictor suprarenin (2 cases) where it had been omitted, increase in the concentration of pontocaine (4 cases), and reinsertion of the needle (5 cases). In 1 case the subarachnoid space was entered; in another this was suspected. No complications resulted, but immediate complete relief of labor pain occurred following injection of less than the usual test-dose. Surgical removal of broken caudal needles was necessary in two cases, the break in each case being near the "neck" of the "hubless" Hingson needle. Neither needle possessed the new "safety-head" designed to prevent disappearance of the needle shaft under the skin. Mild blood pressure fall was recorded in 34 cases, but in only six of these was the fall greater than 30 points systolic. The greatest drop occurred in a mild toxemia in which the pressure fell from 150/100 to 70/40 but it was restored to a safe level by an intravenous infusion of saline and 1 mg. of neosynephrin. Five patients complained of pounding headache during the injection. One complained of momentary chest pain, one of palpitation, and one had nausea and emesis after the first injection. Four had chilly sensations. In three patients severe chills were present after injection, one lasting fifty minutes. Three others developed chills with fever. In one the temperature went to 104° F., and she was disoriented for three hours. In two patients relaxation was so marked that the cervix protruded externally after delivery. Two patients had severe post-partum hemorrhage. There were 13 cases of mild endometritis, 3 of pyelitis and five that required catheterization post partum, which is no more than in cases without caudal anesthesia. Motor loss was present to some degree in 154 cases and in 60 of these it was marked. In most cases the onset of motor paresis was delayed for some time after the first injection. One patient had fecal incontinence for three days. One patient developed anal sphincter relaxation bladder paralysis, and a bilateral foot drop. This patient was a luetic who had received four neosalvarsan injections (2 neo of 0.3 with 0.13 bismuth and 2 neo of 0.6 with 0.13 bismuth) during pregnancy and from whose hair arsenic was recovered post partum. Nevertheless, the paralysis developed during labor. The rectal sphincter gradually regained its tone over a period of ten days but the foot drop improved very slowly and even after nine weeks muscular control is still imperfect.

In our experience labor was not shortened. In six cases labor lasted more than 24 hours after the caudal injections were begun and one of these was a multipara. We were unable to note any evidence of cervical

relaxation due to the anesthetic although there was prompt and complete relaxation of the perineal muscles.

Summary

1. Two hundred cases of continuous caudal anesthesia are presented and discussed mainly from the viewpoint of the obstetrician.
2. Pontocaine-suprarenin-saline solution has proved a safe agent for this method providing 3 to 5 hours of relief from the first dose, and 1 or more hours of relief from subsequent injections.
3. Certain precautions are outlined, but the detailed technique is reserved for another publication. Adherence to a strict regime is advised.
4. Tables are given quoting figures on duration of labor under caudal anesthesia and time required to complete cervical dilatation. We find that cervical dilatation is not accelerated in this series.
5. The incidence of operative deliveries is increased.
6. Several disadvantages of caudal anesthesia are discussed.
7. The results and complications are classified, including $1\frac{1}{2}$ per cent total failures, and 13 per cent additional not completely satisfactory. One hundred seventy-one of 200 cases were completely satisfactory. One prolonged neurological complication is reported.
8. There was no maternal mortality. Fetal mortality was 3.0 per cent.*

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*See Discussion on Symposium on Obstetrical Anesthesia, page 85.

CONTINUOUS CAUDAL ANESTHESIA WITH PROCAINE HYDROCHLORIDE IN 240 OBSTETRIC PATIENTS*

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THE use of continuous caudal anesthesia at the University of Iowa began in August, 1942, and this report is concerned with the first 240 obstetric patients on whom the method was tried. The patients were largely unselected, although the major obstetric complications were avoided. Nine men were responsible for the administration of the anesthetic, a fact which must be borne in mind when the failures in this series are discussed, since it is well recognized that technical proficiency in introducing a needle into the caudal canal is important.

Method

The catheter technique was employed universally. A number 13 gauge, $3\frac{1}{2}$ inch needle was inserted into the caudal canal and a number 5 ureteral catheter threaded through it. Procaine hydrochloride, generally 1.5 per cent in saline solution, was the anesthetic agent, although a 2 per cent solution was used occasionally. The standard dose was 30 cubic centimeters, although varied sometimes to suit individual reaction. As a prophylactic against any possible toxic effects of the drug, 1.5 grains of sodium pentobarbital (nembutal) were given orally prior to introduction of procaine. Believing that the rates of absorption and excretion were more important than the amount administered at any one given time, doses were recorded as milligrams per hour and ranged from 400 to 600. As a working rule, no anesthetic was continued more than 24 hours.

Results

Excellent results (total elimination of pain) were obtained in 68 per cent of the patients. Fair results were obtained in 12.0 per cent, poor in 2.5 per cent, while failure occurred in 16.9 per cent (39 patients). The operator failed to introduce the needle into the caudal canal in 18 instances: In two cases spinal fluid was encountered and the procedure immediately abandoned. In 11 patients the anesthetic was discontinued, 3 times accidentally and 8 deliberately because the patient either was not in labor or was experiencing a prolonged labor. In 8 instances, the cause of failure was not specified. In general, it may be said that anesthesia will always be satisfactory if: (1) the apparatus is placed, and remains, in the caudal canal; (2) if sufficient anesthetic is introduced.

*Read at a meeting of the Chicago Gynecological Society, October 15, 1942.

Effect on Labor

The figures have not been analyzed with regard to the total length of labor, since the series is entirely too small to warrant conclusions in this regard. It is, however, the clinical impression of those who participated in the study that the first stage of labor is somewhat accelerated while the second is markedly retarded. For example 35.4 per cent of the patients in the present series (primigravidas 63.7, multigravidas 10.2) required forceps operation. These figures are considerably in excess of the usually conservative clinic incidence of employment of forceps at the University Hospitals, although indications were not altered. Moreover, the definite clinical impression was obtained that spontaneous rotation from an occiput posterior or transverse position was interfered with, since the incidence of manual or forceps rotations was definitely increased.

Significant blood pressure depressions were noted in a certain number of patients, although this fact was not appreciated at first. In the last 136 patients, depression of systolic pressure below 80 millimeters (Hg) was noted in 13 or 9.6 per cent. This fall was readily combated by the *simultaneous* administration of $\frac{3}{4}$ grain ephedrine sulfate, $\frac{3}{8}$ grain intravenously and $\frac{3}{8}$ grain intramuscularly. Such blood pressure drops are now anticipated through careful observation and ephedrine administered prophylactically, when indicated.

Effect on the Mother

There were no maternal deaths and no postanesthetic paralyses of legs, anal or bladder sphincters by the time (average 10 days) the patient left the hospital. The maternal complications included: Two superficial infections which healed without surgical intervention and which did not cause any neurologic symptoms; 2 subarachnoid punctures followed by immediate abandonment of the procedure; 1 generalized muscle twitching subsiding spontaneously without recurrence despite subsequent reinjections of procaine; 2 patients transiently developing unilateral Horner's syndrome, i.e. mydriasis, widening of the palpebral fissure and slight exophthalmus; 1 catheter cut off. This last accident occurred because the operator, believing the introducing needle was not in the caudal space, withdrew the catheter without first withdrawing the needle. Two centimeters of the catheter were cut off and remained in the caudal canal. No serious operative attempt was made to remove the end of the catheter and the patient suffered no consequences.

Effect on the Infant

There were 2 fetal deaths in a series of 201 patients (240 less 39 failures) but neither death was attributable to the anesthetic. There was one other fetal death but this occurred in one of the 39 cases of failure where no procaine was injected. One hundred seventy-three

(86 per cent) of the children cried spontaneously immediately after birth and in some instances before the shoulders were extracted. Nineteen (9.5 per cent) exhibited a very slight delay in breathing, but in no case more than 2 minutes. Only 3.5 per cent required any resuscitative measures because of asphyxia.

Indications and Contraindications

Continuous caudal anesthesia was administered to certain patients with heart disease, one of whom was a grade III. Her labor was so smooth and the effect on the heart so negligible, it might seem as if this is a very desirable method of anesthetizing cardiac patients.

Because there is practically no effect on the infant, it would also seem that the continuous caudal technique might solve the problem of asphyxia in relation to analgesia and anesthesia for women in premature labor.

The method is contraindicated whenever a test of labor is necessary, since no test can be adequate without the full, voluntary cooperation of the parturient.

Comment

It is premature to predict the future place of continuous caudal anesthesia. The method is time-consuming and there can be no doubt that it possesses potential dangers. These risks may be largely minimized and often eliminated when the method is employed with intelligence and meticulous attention to detail. However, this objection alone should be sufficient to preclude its routine use. The physician employing continuous caudal anesthesia must personally supervise every detail. There should be no delegation of any part of the technical performance to others. On the other hand, it is a remarkable method which comes close to satisfying the requirements of an ideal obstetric anesthetic agent. In selected patients, provided the physician is adequately trained and is prepared to be in constant attendance throughout the course of the anesthetic, it would seem to be a satisfactory method.*

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*See Discussion on Symposium on Obstetrical Anesthesia, page 85.

CONTINUOUS CAUDAL ANALGESIA IN OBSTETRICS

A Commentary

ARTHUR BAPTISTI, JR., B.S., M.D., F.A.C.S., HAGERSTOWN, MD.

AT THE Baltimore City Hospitals, in 1938, caudal anesthesia in obstetrics was subjected to a critical study by a group of resident obstetricians, under my supervision. We confirmed previous investigators' observations, viz.; a single injection of anesthetic agent through the sacral hiatus would produce complete relief from pain for the parturient in active labor regardless of the stage of labor and this analgesia would be accompanied by classical caudal anesthesia and marked perineal relaxation. Such obtundity phenomena persisted for approximately one hour after which time they gradually disappeared. The uterine contractions continued without interruption throughout the period of anesthesia. We also found that if we reinserted the needle in the caudal canal and injected a repeat dose of anesthetic agent when the effect of the previous injection was beginning to disappear, satisfactory anesthesia would continue on for another hour. In other words, we could produce continuous analgesia and anesthesia by a continual administration of anesthetic solution by single injections at appropriate intervals. We studied a small series of cases in which this continuous anesthesia was maintained by repeated injections, beginning at various stages of labor. We hoped to find that labor would progress normally to a spontaneous delivery without pain but we were disappointed. Although we found that cervical dilatation would frequently progress satisfactorily if the presenting part were deeply engaged, if the presenting part were in high pelvis the first stage was sometimes considerably retarded. To our further disappointment we found that in the large majority of cases the second stage was retarded and in almost all cases was arrested. Although some descent usually occurred the presenting part was usually arrested in low pelvis and we were forced to follow one of two courses: delivery by forceps from the arrested station or, allow the patient to recover from the anesthesia and complete the labor by the usual painful second stage. When we followed the latter course we found ourselves dealing with an unmanageable patient who demanded another injection of that "wonderful medicine." This reaction is quite understandable to anyone who has witnessed the dramatic relief of pain with caudal anesthesia. When we delivered these "arrested" heads by forceps we realized that we were rarely performing an "outlet forceps" and too often not a very "low" forceps.

Delivery of all primigravidas by outlet forceps and episiotomy was the established routine of the clinic at the time of our study of caudal anesthesia. I think we were completely aware of what an outlet forceps delivery really means and herein lies a very important issue. When the head has traveled beneath the pubic arch and begins to crown and is then delivered by forceps, such a delivery is correctly an outlet forceps. In this type of delivery the forceps are used for extension but not traction. A head delivered from any higher station ceases to be an outlet forceps and is accomplished principally by traction to bring the head beneath the pubic arch.

Most trained obstetricians feel that elective episiotomy and outlet forceps delivery are justifiable because of both immediate and remote advantages, but these obstetricians also know that elective delivery of a head from a higher station is unjustifiable and constitutes poor obstetric judgment. It is true that a trained operator may deliver from a higher station with a satisfactory outcome when the procedure is indicated and necessary, but he does not elect to do it because he knows that such deliveries are frequently the antecedents of pathologic relaxation of pelvic supporting tissues.

Our experience with caudal anesthesia, therefore, indicated that if the anesthetic were administered somewhere in the middle of labor, we were forced to terminate the labor by what our guided experience dictated was "bad obstetrics." It is true that occasionally a multipara could be encouraged to terminate the labor spontaneously by requesting the patient to bear down when she had a painless contraction, but these cases were the conspicuous exceptions. In most primigravidas with such encouragement the head would not descend to a station from which the delivery could conscientiously be labeled an outlet forceps.

Our conclusions from this study of caudal anesthesia indicated that its use to eliminate first- and second-stage pain was inadvisable because of the interference with the normal mechanism of labor. We concluded that it does have many desirable advantages as an anesthetic for delivery in selected cases when operative delivery is indicated. For such purposes a single injection usually affords sufficient anesthesia time. We also pointed out that the administration of a caudal anesthetic, no matter when administered, is potentially dangerous. And although, by exercising intelligent caution, this danger may be minimized it cannot be entirely eliminated. It seemed to us, therefore, that a caudal anesthesia used as an analgesia is inadvisable. Even as a routine delivery anesthetic it is unjustifiable and should be used only in selected cases. If our factual findings are accurate I believe anyone interested in a higher order of obstetrics will agree with the conclusions. A detailed report of our study and conclusions were duly recorded.¹

We overconfidently ignored our own published counsel and following the completion of our series for publication, the procedure was con-

tinued as a routine delivery anesthetic on the obstetric service. The administration of the anesthetic to approximately our six hundredth case resulted in an accidental intradural injection with sudden respiratory failure. The administration of intratracheal oxygen, artificial respiration and lumbar puncture and withdrawal of spinal fluid (contained anesthetic) resulted in the resumption of spontaneous respiration after twenty anxious minutes. This particular anesthetic was administered by an experienced operator who had taken the usual precautions to exclude intradural and intravenous injection. Our confidence was shaken and caudal anesthesia was discontinued as a routine anesthetic. Our enthusiasm for the procedure was being shared by two other large maternity clinics in Baltimore (The Johns Hopkins Hospital and University of Maryland Hospital) where it was being used cautiously. At the Johns Hopkins Hospital in March, 1940, caudal anesthesia was administered to the one hundredth obstetric patient and two minutes later the patient was dead. All customary safety precautions had been observed. Post-mortem study revealed the presence of the anesthetic solution in the spinal fluid. The procedure was thereafter abandoned at the Johns Hopkins Hospital. The procedure was continued at the University of Maryland Hospital until August, 1940, when a caudal anesthetic was administered and the patient observed for five minutes. The attendant left the patient and returned a few minutes later to find the patient dead. In this case the post-mortem spinal fluid contained no evidence of anesthetic solution. Thus the season of caudal anesthesia was terminated at another hospital when the procedure was abandoned at the University Hospital.

Investigation subsequent to our original report indicates that our conclusions regarding the incidence of comparatively high pelvic arrest represented a sampling error. Hopp² was the first to point out that many labors were not arrested under fractional doses of caudal anesthesia. In 1941, Hopp² published the first report on a series of cases in which he used continuous caudal anesthesia to produce painless labor and delivery. His series was small and apparently attracted little attention. Hopp's principle was highly publicized by Hingson and Edwards in September, 1942,³ and continued with increasing fervor through 1943,⁴⁻⁹ with Hopp's contribution conspicuously ignored. Such persistent zeal is unprecedented in the long line of previous caudal anesthesia enthusiasts. A panoramic view reveals the history of twentieth century obstetrics punctuated with waves of enthusiasm for caudal anesthesia. The present wave of enthusiasm, however, is of such magnitude that it is unquestionably the outstanding topic in American obstetrics today. The reason, I think, is not because of any significant scientific advancement in the application of the principle of caudal anesthesia in obstetrics but the answer lies in the power of the public press. Medical science has not discovered anything new but the lay press has. Expectant mothers all over the country are requesting what

has been misrepresented to them as "safe, painless childbirth." The movement has to some extent stunned the medical profession to the point of clouding its judgment. Even without this influence the average physician is moved beyond reason when he first witnesses the dramatic relief of pain the parturient experiences under caudal anesthesia. Unfortunately, most physicians were caught in this surge of enthusiasm originating in the lay press before they knew what caudal anesthesia in obstetrics was all about and they could not combat it. Their impulse was to jump on the band wagon and ride along. Such reactions, of course, will be only temporary and there are signs on the horizon now indicating that the skies are beginning to clear. Physicians are beginning to awaken to actual facts. Witness the increasing accuracy of interpretation of their own factual findings in the publications of Hingson and Edwards, the chief sponsors of the movement. In their first reported cases they thought they were doing elective forceps deliveries³ and implied that the anesthesia was not interfering with the normal course of labor. However, in their most recent report⁴ they are apparently willing to recognize this interference. They admit, "The incidence of operative obstetrics is increased. No physician should use continuous caudal analgesia unless he is well trained in the use of forceps. The incidence of posterior positions and transverse arrests in midpelvis is increased." And finally, the incriminating admission that "the entire course of labor is altered from the picture described in textbooks."

It is incredible that the leaders of American obstetrics will allow such admissions to go unchallenged. The science and art of obstetrics are built on the concept of the normal mechanism of labor. In our search for the ideal obstetrical analgesia we have always insisted on the rigid adherence to the criterion of "no increase in operative deliveries." Hingson and Edwards would rely on the perineal relaxation to justify their obligatory forceps deliveries. It is true that the muscular relaxation does facilitate the immediate problem of delivery to a degree but caudal anesthesia does not relax the bony pelvic ring. The sequelae of forceps deliveries do not usually become manifest until some time later. Every gynecologist realizes that many of his plastic operations are necessitated because of a forceps delivery done some years before. Hingson and Edwards recommend delivering the patient "when the presenting part can be seen by spreading the vulva."⁶ In this role the relaxed perineum becomes a two-edged sword in that one can visualize the presenting part at a comparatively high station when the relaxed perineal muscles are spread apart. As I witnessed the motion picture on caudal anesthesia which is being shown and watched the depiction of the terminal stages of an axis-traction forceps delivery, I wondered where in the pelvis this head might have been when the delivery was started. That part of the delivery is not shown. I also wondered if that patient will be consulting a gynecologist ten years hence.

Caudal anesthesia is no safer today than it ever was. The present practice of using an indwelling needle or catheter in the sacral canal between injections has done nothing but increase the hazards. Although the ever present danger of vascular collapse probably remains the same, the risk of accidental dural penetration is increased. The hazards of needle breakage and infection have been added. The fact that any therapeutic procedure carries a risk does not necessarily condemn its use in medical practice, the art and science of which is made up largely of the balancing of risks and probabilities. However, the use of such a hazardous procedure *electively* to relieve the usually innocuous pains of labor is unjustifiable. Since the recent advent of continuous caudal analgesia four women have lost their lives because of the procedure per se.^{8, 10-12} There have been other "close calls" reported. There must be other fatal or near fatal accidents which were not reported. Never before has the human nervous system been subjected to the action of such prolonged concentrated anesthesia. The absence of residuals and sequelae remains to be proved. Suggestive evidence of some neurologic damage has already come forth¹³ and this lead is being followed through by experimental animal investigation, as it should be.

When one contemplates the future of continuous caudal analgesia, it would seem important to realize that for many years disciples of caudal anesthesia have frequently appeared on the medical horizon. They have fanatically recommended its use in urology, proctology, gynecology and obstetrics but practically all of these enthusiasts have eventually abandoned the procedure. Some surrendered soon because of the technical difficulty of administration but others who mastered the technique gave up later because of the inherent hazards in the principle. It seems strange that the tragic accidents are so frequently delayed in any one man's experience, but apparently they eventually do occur. I predict they will come to those who are now promoting continuous caudal analgesia. However, even if we assume they will not occur there are other disadvantages to the procedure which preclude its very general application. The procedure is laboriously time consuming. Busy obstetricians, anesthetists, or house officers would have time for nothing else. The financial obligation involved for expert supervision and administration would be prohibitive for most patients.

The fact that the promoters of this movement are conducting a "school" in which a general practitioner, untrained in obstetrics, may administer a few caudal anesthetics to women in labor and then "observe" the delivery of these patients would seem open to serious criticism. Such a practice is a reckless method of evaluating the procedure. The incidence of complications will be inversely proportional to the obstetric judgment and dexterity of those who use it.

The test of time will put continuous caudal analgesia in its appropriate place in obstetrics and until this comes about we must hope that the

minimum number of mothers will suffer harm. Contemplation of the appropriate place of this procedure reminds one of the episode of the elective version of Potter and his disciples who threatened to revolutionize obstetrics by a procedure which interfered with the normal mechanism of labor in order to bring relief to women in labor. The test of time settled the Potter version, appropriately, in the footnotes of the history of American obstetrics. Despite the initial fanfare, I suspect much the same fate for continuous caudal analgesia. Although its occasional use in accurately selected cases may give it some degree of permanence, I predict it will never become generally used in obstetric practice.

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CYCLOPROPANE-PITUITRIN INCOMPATIBILITY

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IT IS surprising to note the paucity of cases of pituitrin shock, especially of those with fatal result, reported in the literature. It is probable that the condition is not as rare as this would indicate, but its occurrence should be kept in mind. The lack of reports is probably due to the failure of the anesthetist or obstetrician to recognize the picture when it presented itself, the diagnosis of pulmonary embolus, shock, coronary occlusion, or anesthetic death being made without considering the possibility of drug susceptibility. These mistaken diagnoses are readily understood since this is often the picture exhibited, but the underlying cause has not been appreciated.

In this paper we should like to point out the basic pharmacologic facts with reports of two cases witnessed.

Pharmacology

Cyclopropane is a very potent hydrocarbon capable of producing surgical anesthesia in concentrations permitting a high percentage of oxygen in the mixture. For this reason, it has come to be demanded by obstetricians when doing cesarean sections, and rightly so, because of the short induction period and the benefits of high oxygenation to mother and child.

Pharmacologically, cyclopropane is a stimulant of the parasympathetic system. It causes bronchoconstriction, which may induce an asthmatic attack in a susceptible patient. It also has a tendency to produce all sorts of cardiac arrhythmias with displacements of the rhythm centers, ranging from bradycardia to ventricular fibrillation.

Pituitrin, an extract of the posterior pituitary gland, has four principal actions. It stimulates the myometrium, causing contraction of the uterus, constricts the capillaries and smaller arterioles by direct action on the muscle cells; stimulates the intestinal musculature to contraction by direct action on the muscle layers; and has a pronounced antidiuretic action by causing maximum reabsorption by the cells in the loops of Henle. The actions primarily affecting our problem are the contraction of the uterus, and the undesirable side effect of constriction of the coronary vessels.⁵ Burstein³ has also pointed out that it intensified the bronchoconstrictive action of cyclopropane, which he found when investigating pitressin, the pressor fraction of pituitrin.

Pituitrin may produce reactions of three types: anaphylactic, cardiac, or respiratory. The first is not particularly dangerous, especially when not in conjunction with cyclopropane anesthesia, and the recovery from the shocklike symptoms with urticaria, itching, and angioneurotic

edema is rapid upon the administration of a few minims of adrenalin. Pituitrin shock due to the action of the pressor fraction on the heart is attributed to coronary constriction followed by myocardial anoxia, dilatation of the heart, decrease in cardiac output, and fall in blood pressure, with sometimes a fatal outcome. The respiratory reactions are signified by bronchoconstriction of varying degree, simulating an asthmatic attack.

Pituitrin is marketed in two forms, which vary only in strength, obstetrical pituitrin having 10 units per c.c., and the surgical form 20 units per c.c. It has been broken up into its fractions, and is obtainable as "pitocin," containing the oxytocic fraction with a very small amount of the pressor fraction, and "pitressin," which is almost purely the pressor fraction with only slight contamination by the oxytocic fraction. Pitocin, rather than pituitrin, is then evidently the drug of choice in obstetrics.

The combined use of cyclopropane and pituitrin is fraught with danger since they are both parasympathetic stimulants. In the circulatory system they have a synergistic tendency toward the production of hypertension and/or cardiac arrhythmias. From the parasympathetic stimulation of the respiratory tract they may produce laryngospasm, crowing, stridor, or bronchoconstriction, which may range from asthmatic wheezing to massive collapse of the lungs. The bradycardia often seen may be due to vagal stimulation, direct myocardial action, or intense coronary constriction.

Case Reports

CASE 1.—Mrs. S. G., a 30-year-old primipara, was admitted to the Adelphi Hospital, Brooklyn, N. Y., on December 6, 1942, with ruptured membranes and irregular pains. She was obese, of a type suggesting an endocrine imbalance, with an ample pelvis. The blood pressure was 120/80, and the physical findings essentially negative except for obesity.

She was in labor until December 10, 1942, with irregular pains of moderate severity, but requiring morphine plus scopolamine sedation because of her uncooperative nature and meager intelligence. The cervical dilatation progressed slowly over this period to 3 cm. At this time a consent for cesarean section was finally obtained.

At 9:25 P.M. on December 10, 1942, anesthesia with a mixture of cyclopropane and oxygen was started, the patient having had no pre-anesthetic medication. A Waters' cesarean section was started at 9:37 P.M., and a normal living child delivered at 10:40 P.M. Ergotrate and pituitrin were then given to contract the uterus and control the bleeding. The pulse, which had been about 110, now rose to 130 and remained between 130 and 140, full and bounding, for the remainder of the operation, which ended at 11:30 P.M. At the close of the operation, when the mask was removed from the patient's face, she became cyanotic, and oxygen was administered, with a rapid improvement in the patient's color. She was watched for about fifteen minutes and then removed to her room. Upon arrival there at 12:00 midnight she was

reacting, became very restless, requiring several attendants to restrain her. Her heart rate had risen to 200, she rapidly became cyanotic, and succumbed at 12:50 A.M., in spite of strenuous supportive measures. Permission for autopsy was not obtained.

On the basis of the clinical findings, we feel that this patient had a massive atelectasis, which probably was precipitated by the combined bronchoconstrictor actions of pituitrin and cyclopropane. The possibility of cyclopropane alone producing this atelectasis is strong, but it was undoubtedly greatly aggravated by the pituitrin.

CASE 2.—Mrs. C. K., a 35-year-old primipara, was admitted to the Lenox Hill Hospital at 6:30 A.M. on November 10, 1943, thirty-five weeks pregnant, with a history of having had severe cramps associated with moderate bleeding the preceding evening. At 8:30 the fetal heart had become irregular and rapid, and a cesarean section was decided upon. Preanesthetic medication of atropine gr. $\frac{1}{150}$ was given at 8:45 A.M.

Induction of anesthesia, using a cyclopropane-oxygen mixture, was started at 9:17, and after an infusion was begun, the operation commenced at 9:29. Up to the time of delivery of a normal living child at 9:40, the pulse had remained fairly constant between 96 and 116, and the blood pressure at about 130/80.

At 9:41, pituitrin, 1 c.c. was injected into the uterus and ergotrate, 1 c.c. given intravenously. At 9:45 the pulse was 132, and then at 9:48 had dropped to 76. At 9:50 the pulse was 176, and morphine sulfate, gr. $\frac{1}{8}$ was given intravenously. At 10:00 the respirations had become somewhat depressed, but responded to coramine and metrazol, 1 c.c. each. At 9:45 small amounts of ether were added to the anesthetic mixture, and the cyclopropane discontinued. At 10:05, 500 c.c. of blood were added to the infusion. From now until the end of the operation at 10:25, the pulse varied markedly between 76 and 164, weak, fairly regular, at times unobtainable.

At 10:40 the patient had fully reacted and was extremely restless, with a feeble rapid pulse, pale, and throwing her arms around, dislodging the infusion. Oxygen was administered intermittently after the close of the operation. Pantopon, gr. $\frac{1}{3}$ was given at 10:50, at which time the patient was pale, with a trace of cyanosis, and oxygen was being administered continuously. At this time, the condition of the patient appeared very grave, and intravenous therapy of blood (500 c.c.) and plasma (500 c.c.) was started in both arms, between 11:00 and 11:15. Her respirations were shallow. Neosynephrin, coramine, metrazol, and adrenal cortex were given intravenously from 11:15 to 11:30 with no result. Her pulse and blood pressure were not obtainable now, and very shallow respirations were being reinforced by positive pressure on the rebreathing bag. At 12:15 the heart beats could no longer be heard, the respirations were maintained with the anesthesia machine and then with an E & J Resuscitator, while intensive stimulation was again given until 12:55, when the patient was pronounced dead.

At autopsy, the only positive findings were some small atelectatic areas in the lungs with no signs of a pulmonary or coronary embolus. There had been no postoperative intra-abdominal bleeding.

In this case, the injection of pituitrin precipitated a severe cardiac derangement. The pulse became uncontrollable, with marked variations, followed by a progressive circulatory collapse. During the close of the operation, the combined effects of ether with a high oxygen con-

centration and stimulants helped maintain the patient's condition, but when the anesthesia was discontinued, she rapidly declined and could not be revived. The ether was given too late in an attempt to stabilize the patient. Undoubtedly, this was a severe form of the cardiovascular type of pituitrin shock due to the combined actions of pituitrin causing myocardial anoxia and cyclopropane disturbing the rhythm centers. The small atelectatic areas in the lungs, found at post mortem, were not enough to have caused this picture.

Discussion

Pituitrin shock has been reported several times in the literature. Bickers² reported an interesting case of an anaphylactic reaction in a multiparous woman at two successive deliveries after the administration of pituitrin, only the second of which was diagnosed and cured immediately with adrenalin. Greene⁴ has reported unfavorable reactions from the use of pituitrin in surgical procedures being done under cyclopropane anesthesia. In a series of seven cases of pituitrin shock in patients undergoing surgical procedures, such as hysterectomy by the vaginal route, where pituitrin was injected into the uterus to minimize bleeding, observed by Adelman and Lennon,¹ there were no fatalities.

In one of our cases, the depression of respiration and bronchoconstrictive effects of cyclopropane combined with the bronchoconstriction of the pituitrin produced a massive collapse of the lungs which was not disclosed while the patient was receiving a high concentration of oxygen. In the other case, the synergistic actions of the cyclopropane and pituitrin served to produce a condition of shock leading to anoxia which was irreversible. It was partially disguised during the anesthesia but once this was discontinued, the status of the patient rapidly became worse, and in spite of strong resuscitative measures, there was a fatality.

Although pituitrin has been used in connection with cyclopropane in many cases where no untoward reactions were noted, this does not absolve the combination of blame. It is in those cases where the patient probably would have had a reaction from pituitrin under any anesthetic that the severe pictures here presented have occurred. Greene⁴ has recommended adding ether to the anesthetic mixture if pituitrin is to be used, depending upon the sympathetic action of the ether to counteract the parasympathetic effects of the pituitrin and cyclopropane.

Comment

Pituitrin shock is greatly accentuated when it occurs under cyclopropane anesthesia, and may cause a fatality. There are two ways to prevent this: first, by using ether along with the cyclopropane; and secondly, by not using pituitrin. Pitocin, the oxytocic fraction of pituitrin, is just as good in causing uterine contraction, without any of

the side effects of pituitrin, and in many obstetric clinics has supplanted it. Ergonovine in any of its forms is an excellent and rapidly acting oxytocic and can be used for this purpose instead of pituitrin. by using either of these alternatives, an extremely unfortunate accident can be avoided.

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INTERSTITIAL ECTOPIC PREGNANCY

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CARL H. DAVIS states that according to modern statistics, ectopic pregnancies vary in incidence from 3.3 cases in 1,000 pregnancies (these being the figures in Schumann's series) to 13 cases in 1,000 pregnancies (Wynn in the Johns Hopkins series).¹ The same author states that pregnancy in the intrauterine portion of the Fallopian tube, so-called interstitial pregnancy, occurs in less than 5 per cent of all ectopic pregnancies.² On the basis of these figures, interstitial pregnancy should occur less than once in 6,000 pregnancies to a maximum of less than once in 2,000 pregnancies. Accordingly, we may consider interstitial pregnancy a relatively uncommon occurrence.³ Because of that fact and in order to show the similarity and dissimilarity in the clinical picture, gravity and termination that may exist in two cases of interstitial pregnancy of about the same period of gestation, the author feels justified in presenting the following two cases.

CASE 1.—Mrs. L. H., colored, 18 years of age, was admitted by ambulance to the medical service of the hospital with the diagnosis of acute food poisoning. Soon after admission, she was transferred to the surgical division, June 16, 1942.

Her family history and past medical history were noncontributory. In December, 1941, she had had a premature eight months' infant.

Present Illness.—Her last period occurred approximately March 28, 1942. On May 8, 1942, while standing, she aborted a six weeks' fetus (unconfirmed statement of the patient). This was followed by bleeding. The bleeding stopped during the night of May 8, but started again on May 9, and she went to a hospital where she remained until May 15, at which time she was discharged with a diagnosis of spontaneous complete early abortion and hypochromic anemia. After returning home, she still felt weak and morning nausea and vomiting continued. On June 16, 1942, at about 1:45 p.m. she developed sudden acute pain beginning in the right lower abdominal quadrant; she felt weak and is said to have fainted. She attributed her sudden distress to some food.

Examination on Admission.—Patient acutely ill, in severe pain with marked pallor and cold extremities; temperature 98.6° F., pulse 84, respirations 20, blood pressure 84/60. Breasts showed colostrum. Abdomen rigid, extremely tender with rebound tenderness, and the maximum point of tenderness is in the right lower quadrant where a mass the size of a walnut can be felt above the pubic crest. Pelvic examination revealed a soft cervix low in the vagina and tender on motion. The fundus uteri was slightly enlarged and displaced slightly to the left of the midline, apparently by the mass on the right.

The laboratory findings were as follows: Urine, negative, blood, hemoglobin 50 per cent, erythrocytes 3,850,000, leucocytes 9,200 with 80 per cent polymorphonuclears and 20 per cent lymphocytes. The Wassermann was negative. Blood immediately typed and voluntary donors sought.

The diagnosis was ruptured ectopic pregnancy, probably in the right tube with the tube plastered against the anterior abdominal wall.

I saw the case shortly after, and immediate operation was ordered.

Operation was done 2 hours and 15 minutes after admission to the hospital, and a little over an hour after transfer to the surgical division. Under cyclopropane and oxygen anesthesia, a right paramedian incision from umbilicus to symphysis was made. Upon opening the peritoneal cavity, there was a tremendous gush of fluid blood under pressure. The mass on the right was drawn out of the abdomen and clamped at its base with two Keith clamps, one on each side (Fig. 1).

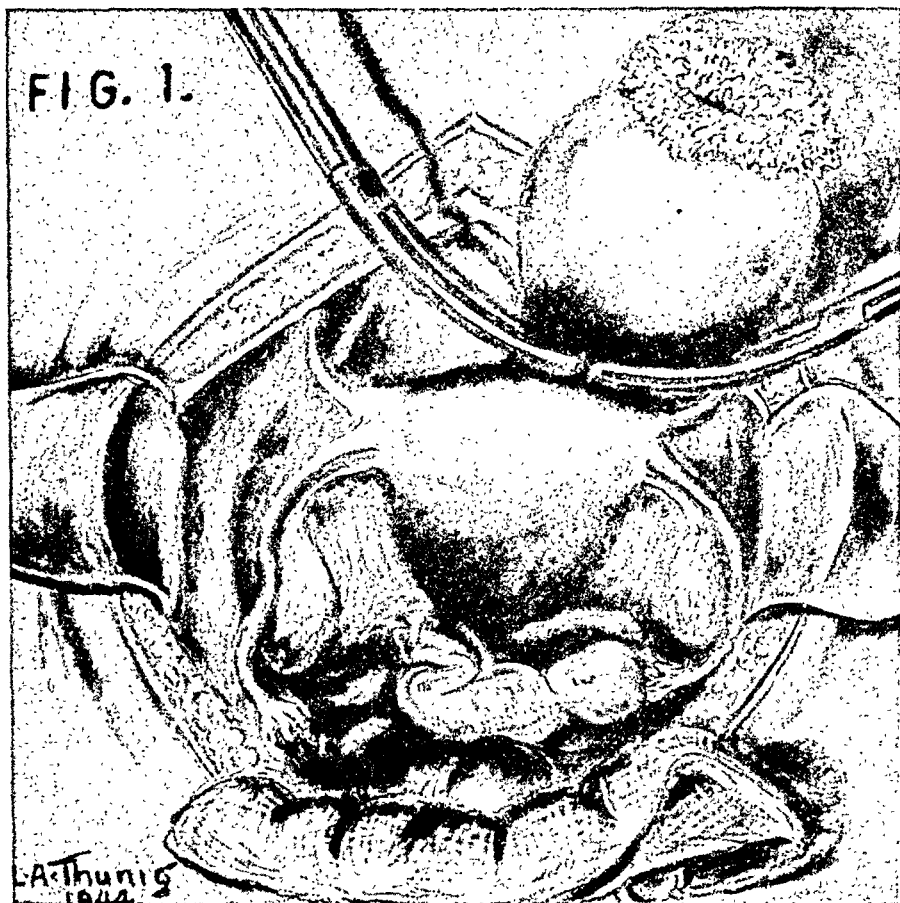


Fig. 1.—Case 1. Ruptured interstitial pregnancy at 11 weeks. Most of the free blood and blood clots, with the exception of the blood clots in the cul-de-sac and deep pelvis, have been removed. Ruptured right cornua with chorion extruded and clamps in place are shown. Note that the extrauterine portions of both tubes are uninvolved. A fetus of about 11 weeks lies among blood clots in the cul-de-sac.

This produced immediate and absolute hemastasis. There was at least a liter or more of free blood and clots in the peritoneal cavity. The mass at the right cornua was about the size of a small orange, it arose mesial to the beginning of the right Fallopian tube proper and the right round ligament, both of these structures being entirely independent of the cornual mass and entirely normal throughout. The uterus was only slightly enlarged; the left tube, left round ligament and both ovaries were normal. The mass had ruptured on its dome for about $1\frac{1}{2}$ inches, chorion extruded from the rent and a ten to eleven weeks' fetus lay unattached on the remaining blood clots in the cul-de-sac. The condition of the fetus indicated that it was in all probability alive until the time of rupture.

The mass was cut off above the clamps; several overlapping mattress sutures were placed beneath the clamps controlling the entire base. The serosal edge of the stump was now sutured with a fine chromic suture. The abdomen was closed in layers, using clips in the skin and silkworm-gut tension sutures with Davey buttons. Operative time was 55 minutes.

The postoperative reaction was good, nevertheless, 500 c.c. of citrated blood were given on the night of operation. There was a moderate febrile reaction during the first five postoperative days with a maximum temperature of 102° F. per rectum. The pulse was excellent throughout being 90 or less with one exceptional rise to 100.

Ten days postoperatively examination showed an abdominal wound healed by primary intention with an entirely negative pelvis other than slight tenderness in the right fornix. The patient was discharged June 27, the eleventh postoperative day.

CASE 2.—Mrs. G. N., colored, 28 years of age, walked into the hospital at 9:30 P.M., Oct. 23, 1942, complaining of left lower quadrant abdominal pain. Her family history was noncontributory. Her personal past history: Seven and again four years prior to admission, she had been told that she had inflammation of the tubes and ovaries. Since June, 1941, she has had a creamy irritating vaginal discharge.

Present Illness.—Her last menstrual period of two days' duration occurred approximately July 28 to 30, about twelve weeks before her present admission to the hospital. On September 10, six weeks later, she had a miscarriage but did not seek medical care. She had cramp-like pains which started after the "miscarriage"; the pains lasted for several hours and disappeared for two weeks; since then the pain has been intermittent and mild.

Laboratory Findings.—Urine, negative, blood, hemoglobin, 72 per cent, erythrocytes, 3,700,000, leucocytes, 22,500 with 84 per cent polymorphonuclears, 15 per cent lymphocytes, and 1 per cent basophiles. The Wassermann was negative.

I examined this patient shortly after admission and the important pelvic findings were as follows: the cervix showed no definite changes in consistency or color and was not tender on motion or otherwise; the uterine fundus was only slightly enlarged and showed no variation in consistency; the right half could be well defined and was essentially negative; perched on top of the left uterine cornua, there was a definite, round, only slightly tender mass about 2 inches in diameter. The fornices, cul-de-sac and rectum were otherwise negative.

*Operation.**—Under cyclopropane, oxygen and ether anesthesia a left paramedian incision was made from umbilicus to symphysis. The uterus proper was not enlarged and was in good position. Both ovaries and the right tube and round ligament were entirely normal; perched on the left cornua of the uterus and arising from same by a broad base was a round mass the size of a tangerine (Figs. 2 and 3). On one side and over the dome of the mass, the omentum was densely adherent and at the firmest point of attachment, it was darkly stained with old blood pigment (Fig. 2). The omentum was ligated and cut just prox-

*This patient's hospital record failed to show that any vaginal examination had been made; furthermore, there was no gross nor microscopic tissue examination made. A preoperative diagnosis of terminated left interstitial pregnancy was made in this case. This was made possible by the history and course, and particularly by a mental comparison of the physical findings in Case 2 as compared to the operative findings in Case 1, both being of almost identical periods of gestation as to duration and occurring a little over four months apart.

inal to its attachment to the mass, and by lifting the mass upward and forward, it could now be seen that the beginning of the extrauterine portion of the left tube was part of the posterior and inferior aspect of the mass (Fig. 3) and on the lower anterior aspect, the left round ligament formed part of the mass, which could be demonstrated by retroverting the uterus. The tube beyond the point of fusion with the mass



FIG. 3.



FIG. 4.

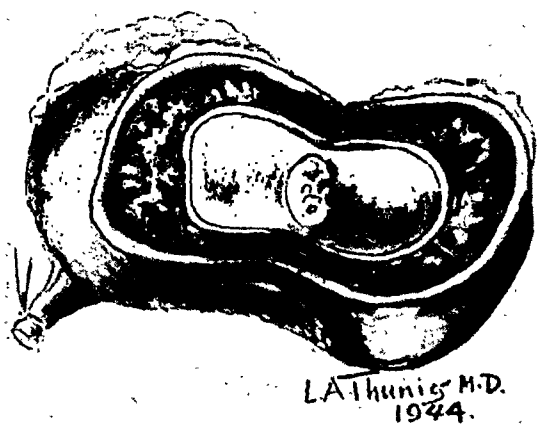


Fig. 2.—Case 2. Round mass at left cornua partly covered by densely adherent and bloodstained (old) omentum.

Fig. 3.—Omentum has been severed and mass lifted. Left tube forming part of cornual mass posteriorly and inferiorly, and left round ligament anteriorly and inferiorly, have both been ligated and cut, the first turn in the knot from a single strand from each ligature denotes method of tying cut ends together. Clamp has been placed across cornua and overlapping mattress sutures placed, the outermost one of which has been purposely drawn slightly heavier, encircles the upper part of uterine artery.

Fig. 4.—Section of left cornua. The stump showing is the tube. Round ligament is also present but not in view. Structures represented from without inward are: adherent omentum, muscular wall of the cornua, blood clot, fibrin and occasional chorionic villus, amnion and 1.3 cm. attached fetus.

was entirely normal; the same held true of the left round ligament. The tube, ovarian artery and a portion of the left broad ligament were doubly ligated about $\frac{1}{2}$ inch from the mass and cut between ligatures; the round ligament was treated in the same fashion. A single curved Keith clamp was placed across the base of the mass just below the level of the stumps of the tube and round ligament (Fig. 3). The distal ends of the round ligament and tube were tied together. The mass was cut off above the level of the clamp. The specimen was sectioned in the operating room and showed a condition as portrayed in Fig. 4. Outer layer consisted of uterine muscle, then came a layer of old organized blood clot with considerable fibrin but only an occasional chorionic villus, then the intact amnion with a 1.3 cm. attached fetus of approximately six weeks. Several overlapping mattress sutures were placed below the clamp, the outermost one being placed to encircle the upper end of the uterine artery (Fig. 3). This formed a groove into which the united ends of tube and round ligament were sutured. The area was then peritonealized by suturing the edges of the lips together over the buried tube and round ligament with a continuous suture.

The patient's postoperative course was uneventful. There was a moderate febrile reaction for the first two days with a maximum rectal temperature of 102.4° F., and a maximum pulse of 120. From the third day on, pulse and temperature were normal and the patient was discharged on the eighth postoperative day with a clean-healed abdominal wall and an entirely negative pelvis and abdomen.

Conclusions

1. Interstitial pregnancies are relatively uncommon.
2. Interstitial pregnancies, even though of about the same period of gestation and similar in some respects, may vary greatly in symptomatology, termination and prognosis.
3. Never accept a patient's statement concerning the occurrence of an abortion unless you personally see the products of conception.
4. These two cases show, as has already been emphasized by so many authors, that every unproved abortion should be suspected of being an ectopic pregnancy until proved otherwise. Observance of this rule would prevent many catastrophes.
5. The presence of a well-defined tumor at the cornua of the uterus with a history suggestive of extrauterine pregnancy should lead one to suspect an interstitial pregnancy.

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SARCOMA BOTRYOIDES

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IN THE rather extensive literature that has grown up on the subject of sarcoma botryoides, McFarland's articles,^{11, 12} together with their associated bibliography, are the most comprehensive to date. As a matter of record and owing to the rarity of the condition in children, the following case is presented for its clinical and pathological interest. The disease ran its course in seven months from the date of onset of symptoms until its termination in August. The patient was inoperable when first seen. Subsequent deep x-ray therapy had no effect in staying the course of the disease.

Present Illness.—About six weeks prior to admission to St. Joseph's Hospital (Case No. 48862) on March 9, 1939, the parents first noted a discharge of pus from the vagina. This persisted and on one or two occasions, the mother noted something protruding from the vagina. This protrusion was not constant; at times it would disappear. The child was taken to several doctors who diagnosed an infection. The discharge persisted and for the past two weeks there has been a small mass persistently projecting from the vagina. The child's appetite has failed markedly. She has lost weight. In the past two weeks the child has had difficulty urinating, having to strain and complaining of pain.

Past History.—The patient was a full-term spontaneous delivery 21 months ago. There were no abnormalities. The child took her formula well and gained steadily. She suffered from repeated "colds" but otherwise gained well and was normal in every respect until the onset of present illness.

Physical Findings.—The child lies in bed appearing pale, feverish and moderately ill. Fulness in lower abdomen with a fixed, firm mass felt in the left lower quadrant. The bladder was moderately distended. Liver and spleen not felt.

Protruding through the vulva was the tip of an irregular cellular mass about 2 cm. in length and 1 cm. in diameter, dark-red and gray in color, firm to the touch, fleshy but not hard. The mass occupied the entire vagina and extended into the right left lower quadrant. On the anterior and posterior aspects of the vulvar portions were several pale, edematous grapelike bodies that could be broken off with the finger. There was no evidence of any cervix and the finger could be swept between the tumor mass and the posterior bladder wall, the latter having an uneven surface as if invaded by the tumor. On catheterization only a few drops of urine were obtained. There was a rather diffuse sanguino-purulent discharge from the vagina.

Biopsy Report.—*Microscopic:* Nine different pieces were selected for microscopic study. Although they vary slightly in structure, they all are made up of predominately myxomatous tissue. Some areas are fairly cellular and early mitotic figures are seen. In some parts the tissue is slightly fibrous with wide hyalinized areas and showing many small, thickened blood vessels. Two of the larger pieces are partly

surrounded by rather thinned-out, stratified, squamous epithelium. There are also areas showing necrosis and hemorrhage.

Diagnosis.—Myxosarcoma (Sarcoma Botryoides).

Autopsy Report.—Path. No. A-3378. (G. B. Kim.) Body is that of a markedly emaciated, white female child. Rigor mortis has not set in. There is marked generalized pallor. There is slight dependent post-mortem lividity. The skin is wrinkled and there is atrophy of the sub-

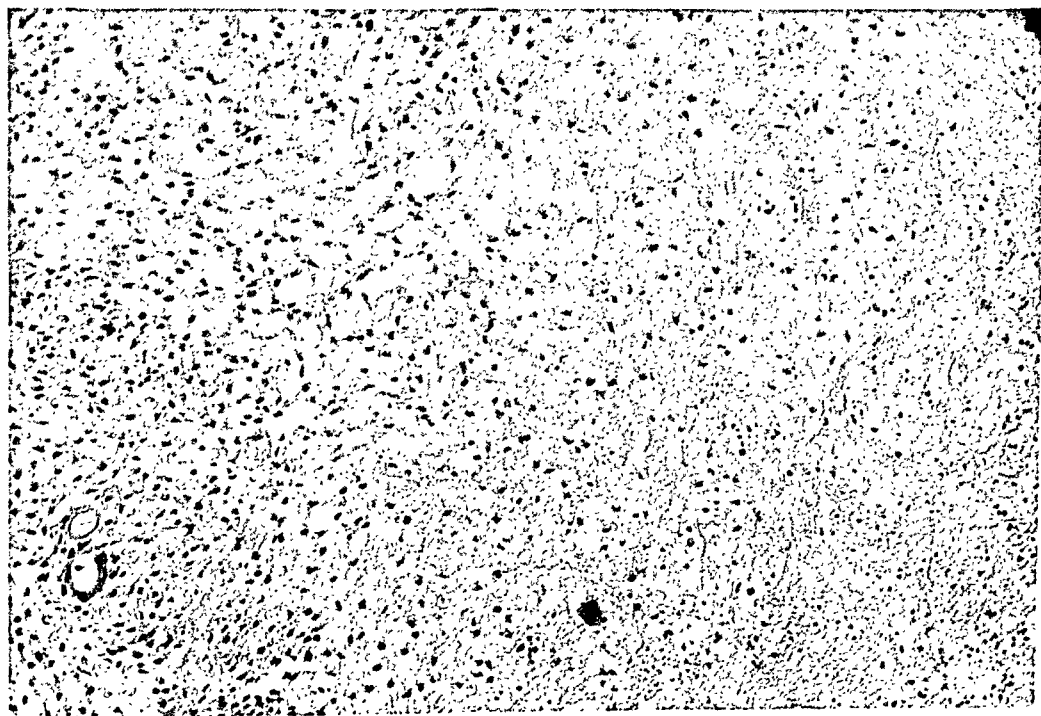


Fig. 1.—Sarcoma Botryoides. Low power photomicrograph ($\times 100$).

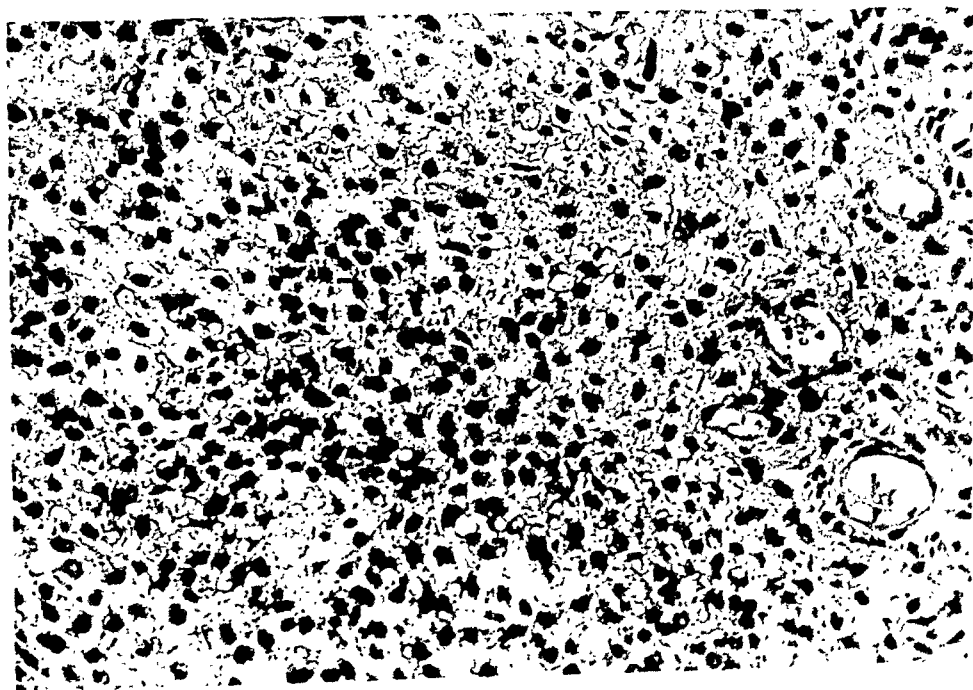


Fig. 2.—Sarcoma Botryoides. High power photomicrograph ($\times 430$).

cutaneous fat tissue. Protruding from the vagina, there is a polypoid, hemorrhagic and edematous mass of tissue which on palpation is found to extend into the vagina and is adherent to the lateral vaginal walls. There are no scars, petechiae or icterus. Edema is not noted.

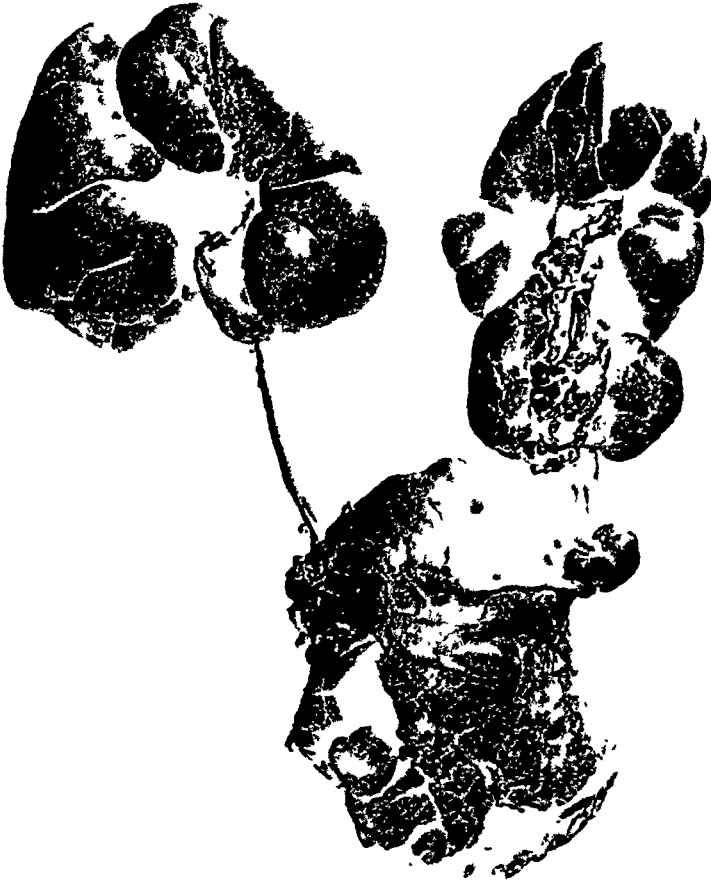


Fig. 3.—Sarcoma Botryoides. Anterior aspect from above downward.

Abdomen.—The skin over the lower abdomen is pigmented, light-brown in color. Distention is more marked in the lower half. The panniculus adiposus is very thin and there is relaxation of the abdominal musculature. The peritoneal cavity contains no free fluid. The peritoneum is smooth and glistening. The greater omentum is adherent to the dome of the bladder. Upon separating it a small amount of purulent exudate is exposed, which is bounded by the omentum superiorly, the dome of the bladder distally and several loops of small intestine posteriorly. There is a perforation in the dome of the urinary bladder from which purulent material exudes and which leads directly into the abscess cavity as described. The liver and spleen are smooth. The liver extends 2 fingerbreadths below the costal margin. The spleen is hidden under the costal margin. The small and large intestines are both moderately distended. The pelvis, after exposure of the abscess cavity, is seen to be filled by a distended bladder and an enlarged uterus. There are several bands of firm, fibrous adhesions between the uterus, bladder and pelvic walls. The uterus is adherent to the bladder and the anterior and posterior cul-de-sacs are obliterated.

Liver.—The organ appears somewhat enlarged, firm, and the capsule is smooth and glistening. On section, it is yellow-brown in color. The cut surface presents a parboiled appearance. The lobular markings are not distinct. The portal fields are seen as pin dots, the central zones are not readily distinguishable. The hepatic and portal vessels are normal. The gall bladder and bile ducts are not noteworthy.

Spleen.—The organ is moderately firm and the capsule smooth and glistening. On section the Malpighian follicles are seen as pinhead-sized grayish areas surrounded by the deep brick-red pulp. The pulp does not scrape. The splenic vessels are normal.



Fig. 4.—Sarcoma Botryoides showing kidneys, lymph nodes, ureters. Posterior aspect with uterus open.

Pancreas.—The lobular markings are distinct. The organ is pale and firm.

Adrenals.—The cortex is of normal width, pale yellow and well demarcated from the gray medulla.

Genitourinary Tract.—Both kidneys are enlarged. The perinephric fat tissue is somewhat edematous and firm. The capsules strip readily, revealing a somewhat finely, granular surface with accentuated fetal lobular markings. Both kidneys are swollen and reddish-gray in color. The cortex is widened and shows scattered hemorrhagic or gray streaks coursing upward from the medulla. They are linear in character and merge with the gray corticomedullary zone. The cortex is moderately well differentiated from the medulla. The medullary pyramids are flattened and the calices dilated. The pelves are markedly dilated on

both sides, as are both ureters. A large amount of urine is present in the pelvis and ureters on both sides. The mucosa of the calices, pelvis and ureters is injected and granular. The dilatation is more marked on the right side. As far as the ureters can be traced to the bladder, they are seen to be dilated.

The bladder is firmly adherent to the anterior vaginal wall and uterus with obliteration of the anterior cul-de-sac. The whole forms a large tumor mass which is removed from the pelvis with some difficulty. The dome of the bladder leads to the abscess described above. The bladder is enlarged and occupied by a tumor mass which invades the anterior and lateral vaginal walls, the cervix, body of the uterus and projects along the vaginal walls to the labia minora, adherent to these on both sides and then projects through the vaginal orifice. The tumor mass is semisoft and composed of lobules of gray-white, edematous appearing tissue which is quite friable and granular. The lobules vary in size from 5 to 20 mm. in diameter, project through the urethral and vaginal orifices in polypoid fashion resembling large bunches of grapes. The base of the polypi is broad, the tips are hemorrhagic. The bladder is filled with tumor and a small amount of purulent exudate. The fornices of the vagina are invaded by a tumor which extends for a short distance down the posterior vaginal wall and all along the anterior vaginal wall. The cervix is patulous and filled by tumor which can be traced along the endometrial cavity. The uterus is enlarged but there does not appear to be any invasion of the myometrium. The tubes and ovaries on both sides are plastered to the pelvic wall by firm fibrous adhesions. The tubes are both dilated, the lumina widely patent and filled with clear fluid. The mucosal folds are flattened. The fimbriated ends are sealed by adhesions. The ovaries are small and undeveloped.

Lymph Nodes.—The left renal hilus contains a large, firm lymph node which is discrete, enlarged to walnut size and well encapsulated. On section, the normal lymphatic structure is gone and is replaced by a yellow, firm tumor tissue. There is no other gross evidence of lymph node involvement elsewhere in the body.

Chest.—Due to the limitations of the autopsy permission, a complete chest inspection was not possible. The pleural cavities contained no free fluid and the pleurae were smooth and glistening. The lungs were soft, well aerated, pinkish in color and on section showed normal lobular architecture. The pericardial cavity contained about 5 c.c. of amber-colored, clear fluid and the pericardium was smooth and glistening. The cardiac chambers were neither dilated nor hypertrophied. The valves and endocardium were normal. The myocardium was firm and brownish-red. The coronary ostia and lumina were patent. The aorta was elastic and smooth. The venae cavae were negative. There were no enlarged lymph nodes.

Anatomical Diagnosis.—

1. Sarcoma botryoides with invasion of bladder, cervix, vagina and uterus.
2. Perforation of fundus of bladder by tumor with localized pelvic abscess.
3. Metastasis to left renal hilus lymph node.
4. Tumor obstruction of both ureters with bilateral hydro-ureter, hydronephrosis and ascending pyelonephritis.
5. Bilateral hydrosalpinx.

6. Parenchymatous degeneration of heart and liver.
7. Extreme cachexia.

Microscopic.—Examination shows rhabdomyosarcoma arising in striated muscle and situated in the uterine wall and arising probably in a teratomatous group from the bladder or uterine wall. (Drs. Gerber and De Ostenay.)

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MYELOGENOUS LEUCEMIA COMPLICATING PREGNANCY*

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EVERY publication on the subject contains the statement: "leucemia is rare in pregnancy," but there is very little discussion of the reasons why.

It is certainly extraordinary that in a disease causing 3,500 deaths annually in the United States alone,¹ and with a steadily increasing incidence,² there should be only 79 cases³ complicated by pregnancy, reported in the entire medical literature.

Are leucemic women sterile? Or/and is there some factor, hormonal perhaps, in pregnancy, which inhibits the development of leucemia? Over 50 per cent of chronic cases reported had leucemia longer than one year before conception occurred;³ at least two became pregnant several times in the course of the disease;^{4, 5} one case became pregnant after x-ray sterilization because of the leucemia.⁶ These cases certainly are not evidence of sterility.

The following is another case in point:

The patient, Mrs. B. T., 22 years old, was first seen on December 14, 1942. She had been married three months and had a two months' amenorrhea, her last menstrual period having begun on October 18, 1942.

She appeared as an obese, rather flabby and dull young woman. She complained of slight headache and morning nausea for the past month. Her past history was negative except for the usual childhood diseases. Her tonsils had been removed at the age of 10. Menstrual periods, onset at age 13, were regular, every 28 days, lasting four or five days.

Her weight was noted as 168½ pounds, blood pressure 110/70, hemoglobin 75 per cent, urinalysis negative except for a faint trace of albumin, blood Wassermann negative. The physical examination revealed no abnormality except overweight and slight pallor of mucous membranes. The pelvic examination revealed an early pregnancy, approximately six weeks. The patient was instructed to report in one week. She did not return, however, until two months later. At that time she still complained of headache and nausea. She had made an attempt to follow dietary instructions, had taken her vitamins and iron; her weight was 165¼ pounds. The gestation appeared to be progressing normally.

Two weeks later, February 21, 1943, she reported having had abdominal pains for three days, and that morning having been seized with a sudden aggravation of the pain accompanied by vomiting. She was seen shortly after at the Woman's Hospital. Temperature 98.6, pulse 80, respirations 20, blood pressure 94/60, slight pallor was noted. No abdominal tenderness was demonstrable, and no masses, outside of the enlarged uterus, but the patient gave a history of acute colicky pain in the left hypochondrium, lasting up to her admission to the hospital.

*Read at a meeting of the Philadelphia Obstetrical Society, March 2, 1944.

A routine blood count taken on admission, showed 68 per cent hemoglobin, 3,400,000 R.B.C. and 106,250 W.B.C. with 24 segmented, 32 stabs, 6 juveniles, 5 lymphocytes and 32 myelocytes. The urine was essentially negative.

During the five days' stay in the hospital, the W.B.C. ranged from 106,250 to 122,250 with myelocytes ranging from 22 to 37 per cent. An x-ray study showed no enlargement of the liver or spleen and no abnormality of the bones. She was discharged with a diagnosis of chronic myelogenous leucemia complicating pregnancy, and given Fowler's solution, initial dose three minims, t.i.d., increasing to fifteen minims t.i.d.

This medication had to be discontinued in three weeks due to the occurrence of diarrhea. The W.B.C. had meanwhile dropped to 88,000. In April, she had a respiratory infection, following which she complained of pain in the left loin radiating to the left thigh. The W.B.C. had risen to 180,000, the urine negative. She was put back on Fowler's solution, Feosol and vitamin capsules—the W.B.C. again dropped to 88,000, the spleen was palpable 1 cm. below rib margin. In her thirty-fourth week of gestation she had another attack of severe abdominal pain, which required morphine for relief. At this time the spleen appeared enlarged and extremely tender, extending 4 cm. below the costal margin. There was marked abdominal distention although the uterine fundus was only 2 cm. above the umbilicus. Fetal movements and heart sounds were normal, however, the fetus lying in right occipitoposterior, the vertex unengaged. Temperature, pulse, blood pressure and urine were normal. The blood count showed 68 per cent hemoglobin, 3,600,000 R.B.C., 126,500 W.B.C. with 23 per cent myelocytes: platelet count 242,000, prothrombin, coagulation and bleeding time normal, Rh factor positive. Medical induction of labor was attempted at this time without success. X-ray treatment was then instituted and given every other day during the period between June 12, and June 21. The areas irradiated were the femora, anterior and posterior, the chest anterior and posterior, 75r. each time. After the fifth treatment, the W.B.C. was 69,500, with 26 per cent myelocytes.

On July 19, 1943, in the fortieth week of gestation, the patient was admitted to the hospital with ruptured membranes, and light, irregular pains. Fetus in R.O.P., fetal heart sounds good, vertex unengaged. Labor progressed very slowly, and lasted 50 hours in all. There was marked abdominal distention throughout the labor and for several days of puerperium. The patient's pelvis was of the funnel type, and the vagina small with a short perineum. The fetal head was arrested in midpelvis and delivery was finally effected with Dewees forceps. Right mediolateral episiotomy was done, but there occurred a third-degree laceration of the perineum. The patient received seconal and scopolamine during the first stage of labor, ether anesthesia, pituitrin and ergotrate at the end of the third stage. Absence of excessive bleeding was noted here as has been noted by several others, and the perineal repair healed perfectly.

The infant, male, 7 pounds, 2 ounces, appeared to be in fair condition at birth. A large caput formation was evident, the cry rather feeble. The second day postnatal, there appeared evidence of cerebral irritation, but this responded well to treatment. A fracture of the right clavicle was demonstrated by x-ray. On discharge, he appeared to be

in good condition, weighing 7 pounds, 11½ ounces. The blood count showed no abnormality at any time.

Even though there was no excessive loss of blood during labor, the entire blood picture showed such deterioration immediately after, that a transfusion of 500 c.c. whole blood was given. The W.B.C. on admission was high, 276,500, with 29 per cent myelocytes, but at the end of labor reached its highest, 323,000, with 32 per cent myelocytes. X-ray treatment was resumed on July 30, 1943. At that time the spleen was noted as being very much enlarged, displacing the splenic flexure of the colon downward and reaching to 3 cm. above the iliac crest. She received four treatments, two to the spleen, two to the femora, but after the last treatment, there was such a sudden drop in the white count (to 12,600) that she was again transfused.

When discharged on August 10, 1943, the patient was in good condition, the only physical abnormality being the enlarged spleen; W.B.C. 10,800, myelocytes 31 per cent. She felt fine and had no complaints until November when she reported pain in the left supraclavicular and shoulder regions. There were no nodes palpable in those areas. She had been taking 45 minims of Fowler's solution daily, but the W.B.C. had been steadily rising and had reached 199,000 with 33 per cent myelocytes. She refused further x-ray treatment, however, and failed to report for her next appointment.

Comment

It does not seem to be the prevailing practice to take a complete blood count early in ante-partum care. Some obstetricians do not do any at all, some take a complete blood count in the last trimester. In the printed forms used in many prenatal clinics, there is space for hemoglobin estimation only.

In chronic leucemia, the symptoms are often vague and confusing. Without blood studies, one would hardly have suspected our patient of being affected by such a serious disease.

How serious is the disease, is well established. How much it is aggravated by pregnancy, is a controversial point.

Kosmak⁷ states that the prognosis in the pregnant is undoubtedly worse than in the nonpregnant.

Moloney and Hefferman⁸ feel that leucemia is uninfluenced by gestation.

Grier and Richter⁹ found exacerbation to be the rule.

To McGoldrick and Lapp³ it seems that the course of leucemia is not greatly, if at all, affected by pregnancy.

More controversial still is the method of treatment.

Grier's⁹ oft quoted statement that, "only two men have seen as many as three cases of leucemia associated with pregnancy," certainly explains why such diametrically opposite stands are taken by different clinicians, particularly in reference to irradiation and to the interruption of pregnancy and the sterilization of the patient.

The conflict of opinion on the latter is obviously due to meager statistics; on the subject of x-ray therapy, those^{3, 10} who decry its use in the pregnant, surprisingly, appear to ignore the fact that the authors¹¹⁻¹³ quoted on the undesirable effects of irradiation, are referring specifically to pelvic, or to fetal irradiation.

Summary

1. A case of chronic myelogenous leucemia complicating pregnancy, treated with arsenic and with x-ray, and delivered of an apparently normal child has been presented.

2. Aggravation of the disease was noted as the pregnancy advanced.

3. Potassium arsenite, although at first effective, later was insufficient to control the symptoms.

4. Irradiation appeared to check the leucocytosis and the pain.

5. The importance of having complete blood counts early in pregnancy is demonstrated, also the necessity of gathering more data for the proper evaluation of methods of treatment in this grave complication of pregnancy.

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1209 SOUTH BROAD STREET

EMBRYONIC CARCINOMA OF OVARY IN A GIRL 13 YEARS OF AGE*

SAMUEL GOLDSTEIN, M.D., F.A.C.S., PITTSBURGH, PA.

(From the Montefiore Hospital)

OVARIAN cancer is comparatively rare in childhood. Kamniker¹ in 1939, reported that out of a total of 2,277 cases of genital cancer seen in the University Woman's Clinic in Vienna, between 1921 and 1933, there were only 157 cases of ovarian cancer, among which were only two cases in patients under 20 years of age, and eight between 21 and 30 years of age. W. Warren Sager² reports that out of 42,864 admissions in the ten years between 1928 and 1938 to the Children's Hospital in Washington, D. C., there was only one ovarian cancer, it being in a girl of nine years of age. Gardner,³ quoted by Sager reported cancer of the ovary in a patient of six years of age. The youngest patient with cancer of the ovary that I found on record was by Forsthius in a girl of three years of age with a complex teratoma of the ovary. Winternitz reported a cystic embryoma of the right ovary in a girl of six years of age. In 1919, H. M. Gerson,⁴ reported in the *Lancet*, a case of papillary cancer of the left ovary in a girl of nine years of age. In 1909, Lahey and Haythorn⁵ reported a case of solid cancer of ovary in a girl of eleven years of age.

Case Report

Miss N. S. (0-1130) was admitted to the Montefiore Hospital on March 2, 1942. She gave a history of being raped in July, 1941. She then missed the August period. In September, six weeks after the attack, she began to bleed. Since that time she has had irregular staining. The only other complaint, in addition to this irregular staining was the gradual enlargement of the abdomen.

Abdominal examination revealed a large symmetrical tumor, extending to about one finger above the umbilicus.

Pelvic examination revealed a hymen that was not intact. A large semicystic tumor extended to about one finger above the umbilicus, probably an ovarian cyst. A smaller mass, the size of a grapefruit was palpated to the left of this large mass, which was thought to be an enlarged uterus. The cervix was normal.

Laboratory Studies.—

1. Friedman pregnancy test was *positive* on two separate tests.
2. X-ray of abdomen, revealed *no* fetal skeleton.
3. Blood count and urine studies showed no abnormality.
4. Blood Wassermann was negative.

A preoperative diagnosis of ovarian cyst with an enlarged uterus was made.

*Presented at a meeting of the Pittsburgh Gynecological and Obstetrical Society, Feb. 7, 1944.

Patient was operated upon March 7, 1942. On opening the peritoneal cavity, a large semicystic mass, the size of a large football, well encapsulated, arising from the left ovary was found. Another mass, the size of a large orange, more solid than the larger mass, and attached by a small pedicle was also present which was densely adherent to the sigmoid and to the omentum. The right tube, ovary, and uterus appeared normal. Palpation of the liver revealed no metastases. A bilateral salpingo-oophorectomy and a hysterectomy were performed.

The patient made an uneventful recovery and was discharged from the hospital on March 22, 1942, three weeks after admission. Deep x-ray therapy was started before the patient left the hospital.



Fig. 1.—Gross specimen of the left adnexal mass, the uterus and normal right tube and ovary.

On September 9, 1942, six months later, the patient was admitted to the hospital with ascites and generalized metastases. She died two days later.

Pathological Report.—(Dr. K. Y. Yardumian.) The specimen consisted of a uterus, two tubes, a large ovarian mass, and ovary. The ovarian mass weighed 12 pounds, cystic in character, well encapsulated. There was another mass the size of an orange attached to the original mass by a pedicle. On sectioning, the large mass showed numerous cysts filled with mucoid substance. In between the cysts there were solid areas with yellowish discoloration. The smaller mass had occasional cysts, mostly solid, sulfury-yellow with multiple hemorrhagic areas. It was very soft and friable and had the gross appearance of malignancy.

The uterus was infantile in size. The endometrium was smooth. No evidence of neoplasm. The tubes showed nothing remarkable. The

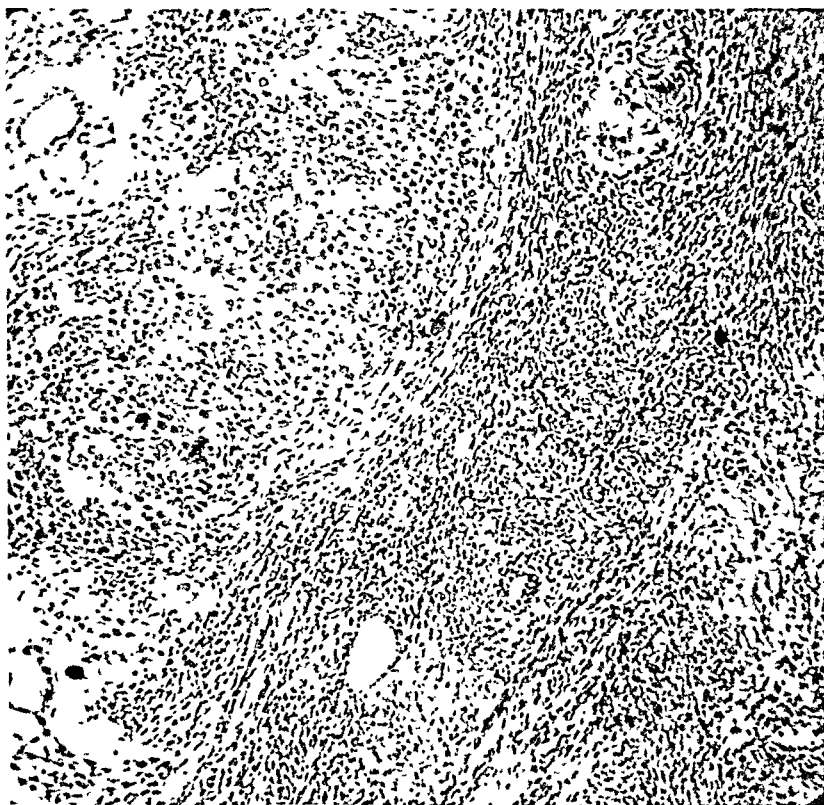


Fig. 2.—Low power magnification ($\times 100$), hematoxylin and eosin stain showing a very cellular structure with loose stroma.

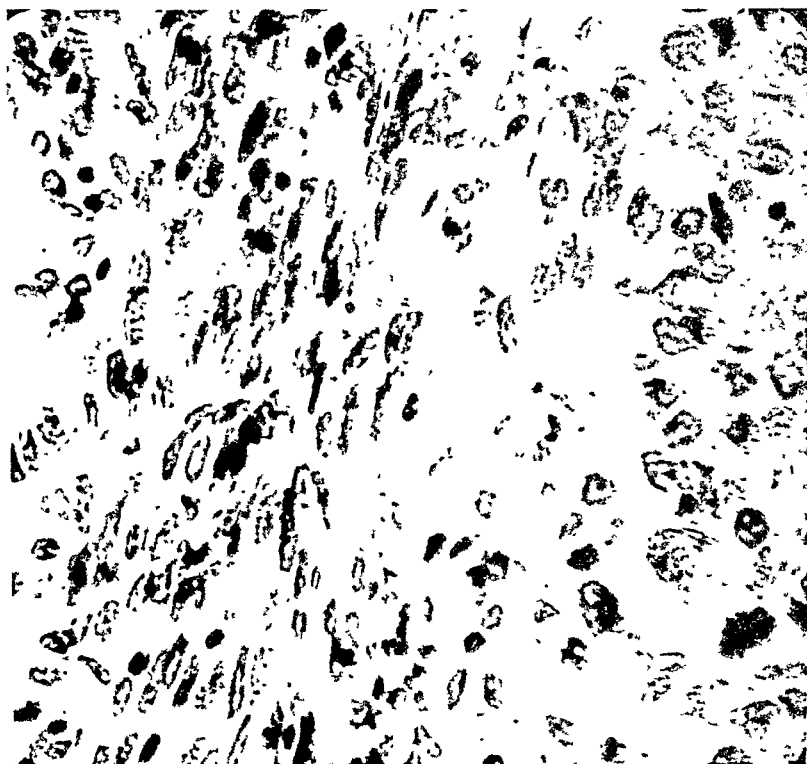


Fig. 3.—High power magnification ($\times 400$), hematoxylin and eosin stain showing undifferentiated cells, mostly pleomorphic. There are numerous atypical mitotic figures. The cells are widely separated by mucoid stroma.

opposite ovary was normal in size and shape, showing numerous follicular cysts.

Sections from the ovarian tumor showed spindle-cell stroma with islands of undifferentiated epithelial cells, pleomorphic in type with mucoid stroma. The blood vessels had very thin walls surrounded by tumor cells. Other portions of the tumor showed glandular structure with mucoid degeneration lined by cuboidal epithelial cells.

Sections of the opposite ovary did not show any involvement with neoplastic changes.

The endometrium also showed normal histologic structure.

Diagnosis.—Embryonic carcinoma, pseudomucinous cyst adenoma of ovary.

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4136 JENKINS ARCADE

FETAL DYSTOCIA FROM A FACE PRESENTATION WITH FORELYING ELBOW

JOHN JOSEPH GILL, M.D., CHICAGO, ILL.

(From the Illinois Central Hospital)

THE following is a case report of a mento-left-anterior position, locked in the grasp of the forelying left elbow, presenting at the pelvic inlet.

This particular dystocia, caused by a malposition of the fetus during a cephalic engagement, is considered of sufficient rarity to merit recording. For that reason I wish to report this case, with the consent of Dr. Ross S. Lang, by whom I was consulted.

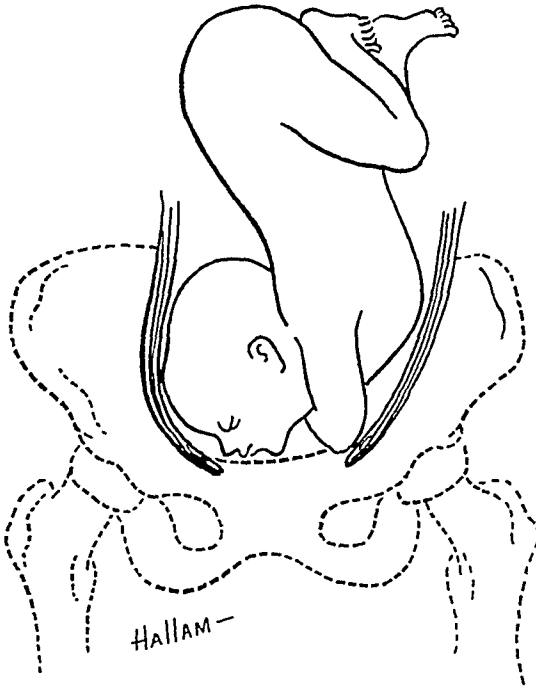


Fig. 1.—Showing relations of child to pelvis.

Mrs. S., aged 21, expected the birth of her second baby on August 10. There was no cephalopelvic disproportion, her prenatal care had been adequate, the past health record was exceptionally good.

On July 29, at 6 P.M., the labor pains started, two hours later she entered the hospital. The pains continued with increasing strength and frequency. After twenty-four hours of labor, the membranes were intact and rectal examination was unsatisfactory.

On July 30, at 6 P.M., a vaginal examination was made. The cervix was found to be completely dilated, the membranes were ruptured artificially, disclosing the reason for the labor without progress. The

forelying left elbow presented under the fetal chin, with the left hand extending over the right shoulder, fixing the head in extreme extention, to the right side of the mother's pelvis, the face toward the left and slightly anterior.

Treatment consisted in releasing the impacted left arm, flexing the head and manually manipulating the presenting parts into an occipito-right-anterior, in which position, delivery terminated in the spontaneous birth of a living male, weighing seven and one-quarter pounds, at 7:25 P.M.

The infant's left arm was swollen and blue from axilla to wrist, for several days; recovery was complete, mother and baby were discharged in good condition on August 8.

A SIMPLE UMBILICAL CORD CLAMP

HARRY S. FIST, M.D., LOS ANGELES, CALIF.

THE cord clamp here illustrated is placed on the cord quickly, prevents bleeding, and may be removed and resterilized when the cord stump has dropped off. It is made from an ordinary safety pin by making two bends in the catch end and pressing both sides of the coil spring end together. The extra pin length is cut off, leaving the tip dull and safer for gloves.



Fig. 1.—Cord clamp.

To apply, slip the open clamp over the cord at about one-fourth inch from the abdomen of the baby and, using the thumb, press the pin to the lock slowly so that the Wharton's jelly will ooze out of the way without cutting the blood vessels. A hemostat may now be placed about one-fourth inch from the clamp and the cord cut between the clamp and hemostat. Antiseptic dressings are applied and the clamp left in position to remain until separation of the cord stump.

This clamp is cheap, easily used, will not open or drop off, and may be easily and quickly made by anyone who has a supply of safety pins, a pair of small pliers and a little patience.

Department of Reviews and Abstracts

Selected Abstracts

Anesthesia, Analgesia, etc.

Carengelo, John: Continuous Caudal Anesthesia in Obstetrics, *South. M. J.* 37: 80, 1944.

Continuous caudal anesthesia with 1½ per cent metycaine was used by the author on 61 patients. He prepares the patient with a small dose of a barbiturate, and gives a cleansing enema. The technique employed was that described by Hingson and Edwards: a steel malleable needle inserted along the roof of the sacrum and connected to a 2-way syringe to facilitate the administration of the anesthetic solution. Potential errors and complications such as subcutaneous instead of extradural insertion of the needle, intravenous injection, subarachnoid injection, broken needles, unilateral anesthesia, and low back pain are mentioned. Contraindications are placenta previa, uterine inertia, hysteria, infections near the sacral hiatus, dystocia, and anatomic defects in the sacral hiatus. Average metycaine dose for all patients was 1.4 grams, the largest dose to a single patient during her labor was 6 grams. Forceps, version and cesarean section were performed without supplementary anesthesia. Post-partum blood loss was minimal. No complications were encountered in this series other than bladder atony. The author emphasizes the importance of observing the bladder during labor as the patient's impulse to void is lost while under anesthesia and overdistention may occur.

WILLIAM BICKERS.

Volpitto, Perry P., Woodbury, Robert A., Abreu, Benedict E., and Torpin, Richard: Continuous Caudal Analgesia in Normal and Complicated Labor: Report of a Death, *South. M. J.* 37: 83, 1944.

Metycaine and Procaine in 1 per cent or 1½ per cent solutions were administered through a #18 rigid steel needle into the caudal canal of 75 patients who were in active labor. Breech deliveries, forceps, craniotomies, a placenta previa, abruptio, and twin delivery were managed under caudal. Throughout labor in 4 patients, the intrauterine pressures were recorded optically according to Woodbury's technique. The effects of caudal analgesia on uterine pressure are shown by tracings. Introduction of the needle into the sacral canal causes increased pressure within the uterus, this tension falls when the analgesic drug becomes effective. The rate and amplitude of contractions diminish in the presence of caudal analgesia. Complete pain relief was accomplished in 51 of the 75 patients, in two patients the needle could not be introduced into the canal, 21 patients had partial relief. Two patients developed infections at the needle site, vomiting occurred in ¼, and there were 4 infant deaths. One maternal death occurred 25 minutes after administration of 30 c.c. of 1½ per cent metycaine. This patient was a negress, obese (200 pounds), luetic, with pitting edema of the lower extremities. Taking the usual precautions to be sure that the needle was properly placed, the solution was injected and 20 minutes later the blood pressure was only slightly below its original level. Five minutes later she collapsed and could not be resuscitated. Post mortem revealed

only generalized passive congestion and evidence of sick-cell anemia in the bone marrow. No meteycaine could be recovered from careful study of the spinal fluid. The baby was rescued by prompt delivery per vaginam. Two rather severe infections occurred in this series, both in obese patients: they were cured by x-ray and sulfathiazole therapy.

WILLIAM BICKERS.

Endocrinology

Harding, Floyd E.: The Oral Treatment of Ovarian Deficiency With Conjugated Estrogens-Equine, *West. J. Surg.* 52: 31, 1944.

A comparison of the conjugated estrogens in a dose tablet of 1.25 mg. of the water-soluble conjugated form expressed as sodium estrone sulfate (Premarin) was made with estradiol benzoate, diethylstilbestrol dipropionate, and estrone. Various ovarian deficiency states were treated such as surgical menopause, the physiologic menopause, hypo-ovarian amenorrhea, vaginal atrophy, and senility. Marked improvement in the general well-being as well as relief of the hot flushes was noted in the menopause group. The amenorrhea group improved in their mental and physical aspects. The author believes that one tablet of this mixed conjugated hormone is more effective than 4,000 I.U. of estrone hypodermically. Vaginal smears could be cornified by oral administration of this hormone. No evidence of toxicity such as that seen in stilbestrol therapy was noted. Uterine bleeding was induced in certain of the menopause cases and delay of the menses was noted particularly in those prone to a hypomenorrhea.

WILLIAM BICKERS.

Novak, E.: Limitations and Possible Hazards of Endocrine Treatment in Gynecology (Editorial), *Am. J. Surg.* 56: 523, 1942.

Although fully cognizant of the comparatively recent tremendous advances in the field of endocrinology as it applies to the female reproductive mechanism, the author carefully appraises the status of endocrinologic therapeutics as it is practiced at the present time. He calls particular attention to the marked discrepancies that exist between the results obtained by animal experimentation and those obtained in the human female. He suggests that a more critical attitude on the part of both laboratory workers and clinicians in formulating their observations will eliminate the tendency to "mislead the uninformed reader and perhaps to disgust those better qualified to detect the fallacies with which they so often abound." He stresses the following points:

1. Since both ovarian hormones, estrogen and progesterone, are now readily available in pure form, there is no excuse for the use of such preparations as ovarian substance, ovarian residue, or corpus luteum.

2. Estrogenic substances do not stimulate the ovary but are only substitutional in the treatment of amenorrhea. They cannot influence cases of sterility.

3. The preparation, stilbestrol, is valuable, especially in the treatment of menopausal symptoms, but should be handled circumspectly.

4. Although there is no acceptable evidence that the estrogenic substances are carcinogenic in the human, the wise clinician will avoid unnecessarily large dosage in patients harboring a precancerous type of lesion or in those in whom a predisposition toward cancer may be suspected.

5. No efficacious gonadotropic principle as applied to the human female is as yet available. Clinical results with preparations of this group have been disappointing.

6. The indiscriminate use of the equine gonadotropic principle in the treatment of sterility is condemned.

7. Treatment of dysmenorrhea and functional bleeding with various hormones is indicated. However, other measures should not be excluded.

8. Androgenic hormone therapy in certain cases of functional bleeding and primary dysmenorrhea is justifiable as is shown by the results obtained. To prevent the troublesome masculinizing symptoms which frequently appear, smaller dosage is recommended, especially in patients who show a tendency toward hypertrichosis.

FRANK SPIELMAN.

Endometriosis

Hurd, R. A.: Some Observations on Endometriosis, *Am. J. Surg.* 53: 61, 1941.

An analysis of 135 cases of endometriosis occurring at the Woman's Hospital, New York, during the past decade is presented. The author believes very strongly that the transtubal implantation theory of Sampson is the most satisfactory as to etiology, and that it should receive the general acceptance of the profession. In most cases endometriosis is associated with, or appears as a complication of some inflammatory or neoplastic condition of the uterus or its appendages, or is the factor responsible for the adhesions seen in fixed retroversion.

The symptoms of endometriosis were rarely typical in this series. They consisted in abdominal pain, backache, and menstrual disturbances, just as in patients manifesting tumors, inflammatory disease or malposition of the pelvic viscera. Dysmenorrhea, which has been stressed by several authors as almost pathognomonic of the disease, was the sole or outstanding complaint of relatively few of the cases here observed, although a majority of patients stated that their symptoms were aggravated at the time of menstruation. Forty per cent of the cases had had previous gynecologic operations, either by laparotomy or from below, and the ratio of nulligravida to parous women was about 5 to 4.

In treatment, operation is the method of choice although radiotherapy may also be used. The author tends to favor radical excision of the pelvic viscera when the involvement is marked. In young women more conservative procedures may be performed especially where preservation of the menstrual and childbearing functions are desirable.

FRANK SPIELMAN.

Gynecology

Phaneuf, Louis E., Heffernan, Roy J., and Kasdon, S. Charles.: Functional Urinary Incontinence in Women, *New England J. Med.* 229: 743, 1943.

The authors report a series of twenty-three cases operated upon by the Kennedy technique. Three drawings help to illustrate and to clarify the essential points of the operation.

Either marked improvement or complete late recovery of the bladder function was obtained in eighteen cases, or ninety-one per cent.

The two failures which occurred are presented, and possible causes for failure are discussed.

JAMES P. MARR.

Schwartz, F. L.: Uterine Prolapse, *Am. J. Surg.* 53: 111, 1941.

By utilizing x-ray in conjunction with a Hyams cannula introduced into the cervix, the author attempts to correlate symptoms referred to the pelvis and ostensibly due to prolapse, with the degree of actual prolapse present. This is accomplished by taking x-ray plates with the cannula in place pushing the cervix high into the pelvic cavity, and again after the cervix has been pulled down by means

of a tenaculum devised by the author. Measuring from a fixed point on the symphysis pubis, the degree of excursion of the cervix by this technique determines the degree of prolapse. In a series of 25 cases studied, the average mobility in the group without symptoms was 2.6 cm. and the average "low" above the symphysis, 5.5 cm. In the group with symptoms, the average mobility was 5 cm. and the "low" point above the symphysis, 1.2 cm. The author concludes that a "low" point less than 3.5 cm. together with mobility greater than 4 cm. indicates uterine relaxation of sufficient degree to be capable of causing symptoms. Uterosalingography may be utilized while performing this procedure if additional information regarding the uterus and adnexa is desired.

FRANK SPIELMAN.

Harrell, W. B.: The Pelvoscopic Method of Uterine Suspension, *Am. J. Surg.* 62: 149, 1943.

A method of performing a Gilliam suspension of the uterus using the "pelvioscope" is described. The instrument is a modified endoscope whose barrel is 11 cm. in length and 1 cm. in diameter, and whose obturator has a tapering triangular cutting point extending about 4 cm. below the sheath. Light is obtained by means of a small electric light which is fitted to the cylinder. A dull hook about 18 cm. long is used to grasp the round ligaments in performing the operation. The instrument is introduced into the peritoneal cavity through an incision 1 cm. long on each side of the midline. The obturator is then removed, the round ligaments identified and brought into the wounds to be sutured above the fascia. The author believes this procedure "to have moderate usefulness in that it may be performed successfully on those cases of uncomplicated retroversion and retroflexion that appear to be producing symptoms." The patients may become ambulatory the first postoperative day and the period of hospitalization reduced to one or two days.

FRANK SPIELMAN.

Jeffreys, E. M., and Graffagnino, Peter: Incidence, Treatment and Prevention of Hydatid Mole and Chorionepithelioma, *West. J. Surg.* 52: 29, 1944.

During a ten-year period there was an incidence of 1 hydatid mole to every 3,049 pregnancies. In general the symptoms were bleeding, painful contractions, passage of vesicles, nausea, headache, and dizziness. Two patients had recurrent moles. About 5 per cent of cases with hydatid mole will develop chorionepithelioma; hysterectomy on moles of questionable malignancy will reduce the incidence of malignant degeneration. The author quotes Hertig to the effect that mole is much more common than generally thought, occurring often as a small area on the placenta in spontaneous abortions. About 50 per cent of spontaneous abortions are the result of defective ova and about 60 per cent of these have shown some hydatid change in the placenta. To prevent malignant or hydatid degeneration of placental tissue following abortion, the author recommends dilatation and curettage on all abortions of 3 months' gestation or less. Treatment of hydatid mole consists of thorough curettage with careful study of the scrapings. Monthly Friedman tests should be done and a persistent positive is indication for radical surgery. The frequency of hydatid change in spontaneously aborting ova contraindicates the enthusiastic use of progesterone to prevent abortion. In the study of pathologic material, it must always be remembered that trophoblastic tissue is normally proliferative and invasive, and is frequently borne to the lungs following delivery, and this must not be confused with the metastasis of a malignant chorionepithelioma.

WILLIAM BICKERS.

Boyce, Frederick F.: *The Diagnostic Confusion Between Acute Appendicitis and Pelvic Inflammatory Disease*, New Orleans M. & S. J. 96: 303, 1944.

Difficulties in the differential diagnosis between acute appendicitis and acute pelvic inflammatory disease have been intensively studied. The author has analyzed 60 cases with acute pelvic inflammation who were operated upon with the diagnosis of acute appendicitis, and he has studied 46 cases of acute appendicitis which were mistakenly diagnosed as inflammatory disease and operation was therefore postponed. In the first group, the unnecessary emergency operations resulted in no deaths, while in the second group, the error in diagnosis was the cause of 3 deaths. Because the patient has inflammatory disease does not mean that the patient cannot have acute appendicitis as well. Right-sided pain as the first symptoms suggests appendicitis but many of the inflammatory cases had a similar history. Pain arousing the patient from her sleep is more typical of appendicitis. Coincidence of pain with the onset of vaginal bleeding was the same in both groups. Dysuria is much more common with inflammatory disease but does occasionally present itself as a symptom in appendicitis. Chills are much more common in the former. The temperature, leucocyte count, and sedimentation time are not helpful. Backache is much more typical of inflammatory disease and in its absence the author hesitates to make a diagnosis of that disease. In summary, the author emphasizes that acute appendicitis is a complex clinical syndrome which may simulate acute inflammatory disease to such a degree as to make differential diagnosis impossible. In such cases the abdomen should be opened and the appendix removed. If an acute inflammatory disease is found, then the peritoneal cavity is sprinkled with sulfanilamide and closed.

WILLIAM BICKERS.

Hardt, H. G., and Seed, L.: *The Diagnosis of Torsion of the Pedicle of an Ovarian Cyst*, Am. J. Surg. 56: 598, 1942.

The records of 69 patients with torsion of the pedicle of an ovarian cyst who were operated upon at the Cook County Hospital, Chicago, from 1925 to 1940 inclusive, are reviewed. Sixty-nine per cent of the twisted cysts were of the simple type, including follicular cysts, corpus luteum and hemorrhagic cysts. The various symptoms which aid in diagnosis are discussed, including pain, nausea and vomiting, menstrual irregularities, abdominal tenderness, rigidity, and the presence of a mass. Radiation of pain down the thigh of the affected side is stressed. X-ray may aid in diagnosis by visualizing calcareous deposits in ovarian neoplasms especially dermoids. Where ordinary pelvic examination is unsatisfactory, examination under anesthesia is suggested.

FRANK SPIELMAN.

MacManus, J. E., and Moore, J. A.: *The Value of the Fractional Hormonal Tests in the Diagnosis of Hydatidiform Mole*, Am. J. Surg. 56: 669, 1942.

The authors present 2 cases of hydatid mole both of which were diagnosed pre-operatively by means of the Aschheim-Zondek and Friedman tests in high dilution. In the first case, positive Friedman tests were obtained with 20 c.c., 0.025 c.c., and 0.001 c.c. of urine. In the second case, the Aschheim-Zondek test was positive in dilutions of 1 to 50, 1 to 100, and 1 to 200. The Friedman test, however, was negative with 0.025 c.c., 0.005 c.c., and 0.001 c.c. No explanation is offered for the negative reaction in the second case.

FRANK SPIELMAN.

McLaughlin, E. F.: Ovarian Lesions Simulating Appendicitis, *Am. J. Surg.* 57: 114, 1942.

The ovarian lesions which most frequently give rise to symptoms suggestive of appendicitis are ruptured Graafian follicles, follicle and corpus luteum cysts, and bleeding corpora lutea. A series of 49 cases with ovarian lesions simulating appendicitis were studied. Of these, 21 showed freshly ruptured cysts at operation, 17 showed unruptured cysts, 3 showed both appendicitis and cyst rupture, and 8 were not operated upon. All of the patients were white, an observation which other authors have repeatedly stressed. The average age was about 25 years, and 70 per cent of the women were unmarried.

Differential diagnosis is carefully discussed, especially in relation to acute appendicitis, pelvic appendicitis, and chronic or recurrent appendicitis. At operation partial resection of the ovary was performed in 37 cases, oophorectomy in 3 cases, and salpingo-oophorectomy once. There was no mortality. As the result of careful follow-up, the author concludes that ovarian partial resection will give freedom from further symptoms in 82 per cent of cases. He particularly stresses the necessity for operation where appendicitis cannot be ruled out.

FRANK SPIELMAN.

Hochman, S.: A Review of 500 Gynecologic Patients With Urinary Symptoms, *Am. J. Surg.* 52: 472, 1941.

As the result of the study by urethroscopy and cystoscopy of 500 gynecologic patients presenting various urinary complaints, the author reaches the following conclusions: Urinary symptoms in the great majority of female patients have their origin in the vesico-urethral junction. The female patient with urinary symptoms should have a meticulous examination of the urethra, bladder neck and bladder. The correction of gynecologic disease and abnormal physiologic changes is frequently followed by alleviation of the urologic symptoms. Dilatation of the urethra is of definite value in the treatment of diseases of the vesico-urethral junction. Hydrotherapy, general hygienic measures and proper sedation should accompany local treatment. The term, "cystitis," so frequently used as a diagnosis to cover urinary symptoms, should be replaced by that applicable to the specific pathology found.

FRANK SPIELMAN.

Castallo, M. A., and Feo, L. G.: Ovarian Hemorrhage, *Am. J. Surg.* 53: 82, 1941.

The authors propose the term, "oophorrhagia," to denote bleeding from an ovulatory site severe enough to produce clinical symptoms or signs. They present a study of 28 cases seen at the Jefferson Medical College Hospital from 1930 to 1939 inclusive. Twenty-six of the cases were operated upon at which time the diagnosis was either established or confirmed. The condition was correctly diagnosed in only 5 instances or 17.8 per cent. It is interesting to note that all of the cases occurred in white women although 50 per cent of the patients admitted to the hospital are colored. Sixty-four per cent of the women were nulliparous and more than half were between 15 and 25 years of age. The operative procedures most commonly performed were oophorectomy, salpingo-oophorectomy, or partial resection of the involved ovary. Conservatism at operation is stressed.

FRANK SPIELMAN.

O'Neill, Thomas: Congenital Absence of the Vagina Treated by the Baldwin Technique, *Brit. M. J.* 4327: 46, December 11, 1943.

Several of the plastic methods of reconstruction of the vagina are mentioned. The author describes a case in which the small bowel was used to make an artificial vagina with a successful result.

WILLIAM BERMAN.

Newborn

Lewis, J. M., Bodansky, Captain O., and Shapiro, L. M.: Regulation of Level of Vitamin A in Blood of Newborn Infants, *Am. J. Dis. Child.* 66: 503, 1943.

The authors studied a series of 108 infants throughout the newborn period to determine the cause of the low concentration of vitamin A in the blood during the first three days of life. This deficiency led the authors to believe was due to the failure of the liver to mobilize and store adequate amounts of the vitamin. In as much as no pathologic disorder was produced, the authors did not recommend frequent administration of vitamin A concentrate.

JAMES P. MARR.

Ingraham, Frank D., and Matson, Donald D.: Subdural Hematoma in Infancy, *J. Pediat.* 24: 1-38, 1944.

This lesion is most frequently seen during the first six months of life. Trauma during labor or delivery, or head injuries following are nearly always a factor in producing this entity.

At the Children's Hospital during the past six years, the staff together with the neurosurgeon have confirmed the diagnosis by subdural puncture in ninety-eight patients. Ninety-four of these bilateral burr holes were made. Ninety-four craniotomies were performed with an operative mortality of 5.3 per cent and a case mortality of 7.9 per cent. Fifty-seven patients adequately followed for periods ranging from six months to five years of age, disclosed 23 per cent were retarded or grossly deficient, while 77 per cent were not only asymptomatic, but showed normal behavior.

The authors give in considerable detail the signs and symptoms which indicate subdural hematoma and a carefully planned and detailed technique for surgery is outlined.

Favorable results led the authors to urge the general practitioner, the obstetrician and pediatrician to diligently seek for more such cases, as the frequency with which subdural hematoma is found depends on the intensity for its search.

JAMES P. MARR.

Eichwald, E. J.: Case of an Omental Cyst in a Three Weeks' Old Female Causing Fatal Ileus, *Am. J. Surg.* 53: 181, 1941.

According to the author this is the youngest case of omental cyst on record. It occurred in a 3 weeks' old female infant causing ileus with gangrene of the bowel terminating in death. The cyst measured 4 by 5 cm. and was composed of 2 layers. It was probably lymphogenous in origin.

FRANK SPIELMAN.

Pregnancy: Complications

Hull, Edgar: Tuberculosis and Pregnancy, *New Orleans M. & S. J.* 96: 321, 1944.

It is estimated that active tuberculosis is present in 0.7 per cent of pregnant women. There are 32,000 pregnancies in this country each year complicated by this disease. However, the author feels that pregnancy has little effect upon the course of tuberculosis. Since the disease has its highest mortality during the most reproductive years, it stands to reason that many deaths will occur either during or just after a pregnancy. There is much evidence to support the thought that tuberculosis is neither affected favorably or unfavorably by pregnancy. The prognosis depends upon the stage of the disease and its treatment regardless of the pregnancy. The above conclusions are based upon the opinions of other quoted authors

and the study of 29 pregnant women with active tuberculosis. Of this group one woman died, 28 were presumably healthy following delivery and there were delivered to these women during the years of this study 34 healthy children. It may be concluded that pregnancy has little effect upon the course of the disease. The mortality rate in pregnant or recently pregnant women due to tuberculosis is not greater than nonpregnant women of similar ages. No patient has been aborted for active tuberculosis during the last 9 years at the Louisiana State University Hospital.

WILLIAM BICKERS.

Schenck, S. B., and Rader, M. J.: Spontaneous Rupture of Uterus in Fourth Month of Pregnancy, *Am. J. Surg.* 52: 494, 1941.

This is a report of a case of spontaneous rupture of the uterus in the fourth month of pregnancy. The rupture occurred in the region of the right cornu at the site of a salpingectomy performed 16 months previously. It is also an example of transperitoneal migration of the ovum, since the corpus luteum was found in the right ovary.

FRANK SPIELMAN.

Cohen, Raymond C.: Effect of Pregnancy and Parturition on Pulmonary Tuberculosis, *Brit. M. J.* 4328: 75, December 18, 1943.

Certain deductions are made from a study of 100 cases of pulmonary tuberculosis complicated by pregnancy. These are all sanatorium cases. It was found that pregnancy and labor per se, rarely exert any harmful effect on the progress of a woman known to have suffered from pulmonary tuberculosis and therapeutic abortion need not be resorted to. Active pulmonary disease is seldom accelerated by pregnancy and labor, and with treatment under favorable conditions, pregnancy has been little more than an incident in their tuberculous career. Careful consideration is given to the fact that these cases are all sanatorium patients, and the added discomforts of a life outside of a sanatorium which may precipitate a breakdown are absent. With proper care and treatment, the tuberculous woman may be allowed to proceed safely to term.

WILLIAM BERMAN.

Cohen, R. R.: Congenital Malaria, *Obst. y ginec. Latino-Am.* 1: 431-436, 1943.

From an extensive experience in malaria district, the author comes to the conclusion that congenital malaria is a reality. He observed that mothers with plasmodium in the peripheral blood, bear children who had plasmodium in their peripheral blood, in the placenta and in the umbilical cord. Some of the newborn babies have fever and others die shortly after birth.

The author failed to find evidence of injury in any of the placentas of malarial babies and therefore he maintains that the passage of plasmodium takes place in healthy placentas. He prescribes euquinine during pregnancy in women who have malaria. This does not lead to abortion but on the contrary helps to prevent abortion which malaria has a great tendency to produce. In cases of toxemia, quinine must be used with great caution because of its tendency to produce hemolysis.

J. P. GREENHILL.

Sterility, Fertility, Contraceptives

Birnberg, C. H., Kurzrok, L., and Weber, H.: Effect of Pregneninolone (Ethinyl Testosterone) Upon Human Cervical Secretion, *Am. J. Surg.* 57: 180, 1942.

Pregneninolone (pranone) was given to 6 patients all of whom manifested a negative semen penetration test, and 5 of whom showed an acid cervical secretion

(hydrogen ion concentration from 5 to 6). Following the administration of the material, the secretion became alkaline and the semen penetration test positive in 5 of the cases. Three subsequently became pregnant. One case was unchanged. The pregneninolone was administered in 10 mg. doses twice daily.

The semen penetration test consists in putting one drop of semen and cervical mucus upon a slide so that the surfaces become contiguous when covered by a glass cover slip. The test is positive if columns of spermatozoa can be seen microscopically in the cervical mucus. The test is negative when the spermatozoa are repelled by the mucus so that they cannot penetrate it.

FRANK SPIELMAN.

Murroy, E. G.: Gonadal Stimulation by Ascorbic Acid, *Bol. Soc. de obst. y ginec. Latino-Am.* 1: 437-451, 1943.

In 18 cases of deficient spermatogenesis, the author prescribed ascorbic acid. The increase in the motility and viability of the spermatozoa and the decrease in the number of abnormal forms, led the author to recommend this therapy.

J. P. GREENHILL.

Sharman, Albert: Some Recent Studies and Investigations in Sterility, *Proc. Roy. Soc. Med.* 37: 67, 1943.

The author reviews four aspects of the problem which he has investigated, namely, (1) on the estimation of tubal patency; (2) on anovular menstruation as assessed by endometrial biopsy; (3) on endometrial tuberculosis; and, (4) on the causation of tubal occlusion. He concluded that an isolated or occasional finding of apparent nonpatency may occur, and this, equally in anesthetized and nonanesthetized subjects, and the result of a single insufflation showing apparent nonpatency, cannot be depended upon. Among 115 patients who became pregnant, 29 had been diagnosed as having nonpatent tubes as a result of a single insufflation. The finding of nonpatency may occur at any time in the cycle. Tubal insufflation should be repeated several times before a diagnosis of nonpatency can be made.

It was found in this study that anovular menstruation is, therefore, a major infertility factor when it occurs, although the actual incidence is low. In reference to tuberculosis, it was found that although the incidence of the disease is minimal, endometrial tuberculosis is 15 times more common in sterile women than in those who are not. The authors feel that there is very little positive proof that, apart from gross tubal damage, gonococcal salpingitis is a common cause of tubal occlusion. The general condition appears to be that the gonococcus is seldom responsible for the occlusion of tubes which are not palpably thickened. Since the author found unsuspected subclinical endometrial tuberculosis in 5 per cent of sterile women, and since this is invariably secondary to tubal tuberculosis, it is highly probable that subclinical tubal tuberculosis is present in at least 5 per cent of sterile women. This is offered as an explanation for tubal blockage.

WILLIAM BERMAN.

Society Transactions

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 15, 1943

SYMPOSIUM ON CAUDAL ANESTHESIA

The following papers were presented:

Analgesia and Anesthesia for Obstetrics Inhalation Methods. W. Allen Conroy, Captain, M. C., A. U. S. (For original article, see page 81.)

Local Anesthesia. Henry Buxbaum, M.D. (For original article, see page 90.)

Continuous Caudal Anesthesia With Pontocaine: Obstetrician's Viewpoint. James E. Fitzgerald, M.D., James M. Thomson, M.D., and Hugh O. Brown, M.D. (For original article, see page 94.)

Continuous Caudal Anesthesia With Procaine Hydrochloride in 240 Obstetric Patients. William F. Mengert, M.D. (For original article, see page 100.)

PHILADELPHIA OBSTETRICAL SOCIETY

MEETING OF MARCH 2, 1944

The following papers were presented:

Myelogenous Leucemia Complicating Pregnancy. Helen M. Angelucci, M.D. (For original article, see page 125.)

Cesarean Section Morbidity and Septic Mortality in Relation to the Type of Operation. Clarence C. Briscoe, M.D. (For original article, see page 16.)

The Prognosis and Management of Premature Rupture of the Membranes. Edward H. Bishop, M.D. (For original article, see page 45.)

Item

Directory of Medical Specialists

The third edition of the Directory of Medical Specialists listing names and biographic data of all men certified by the fifteen American Boards is to be published early in 1945. Collection of biographic data of the Diplomates certified since the 1942 edition, and revision of the older listings in that volume are now going forward rapidly. Diplomates are requested to make prompt return of notices regarding their biographies as soon as possible after receiving the proper forms from the publication office soon to be mailed to them.

Erratum

Dosage of Ethinyl Estradiol

In the article by Robert A. Lyon, entitled "Management of the Climacteric With Ethinyl Estradiol," published in the April, 1944 issue, page 534, the sentence, "attempts to decrease the dosage to 20, 30 or 40 milligrams of ethinyl estradiol daily resulted in the reappearance of flashes in most patients who had been controlled with 50 milligrams," should read as follows:

"attempts to decrease the dosage to 0.02, 0.03, or 0.04 mg. of ethinyl estradiol resulted in the reappearance of flashes in most patients who had been controlled with 0.05 mg."

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

- American Gynecological Society.** (1876) *President*, Edward A. Schumann, Philadelphia, Pa. *Secretary*, Howard C. Taylor, Jr. 842 Park Ave., New York, N. Y. Next annual meeting, June, 1945.
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons.** (1888) *President*, W. R. Cooke, Galveston, Texas. *Secretary*, James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 1944.
- Central Association of Obstetricians and Gynecologists.** (1929) *President*, John H. Moore, Grand Forks, N. D. *Secretary-Treasurer*, W. F. Mengert, Dallas, Tex. Annual meeting not announced.
- South Atlantic Association of Obstetricians and Gynecologists.** (1938) *President* Oren Moore, Charlotte, N. C. *Secretary*, T. J. Williams, University, Va. Annual meeting cancelled.
- A. M. A. Section on Obstetrics and Gynecology.** *Chairman*, Philip F. Williams, Philadelphia, Pa. *Secretary*, William Mengert, 2211 Oak Lawn Ave., Dallas Tex. Next meeting, New York City, June, 1945.
- New York Obstetrical Society.** (1863) *President*, W. E. Studdiford. *Secretary*, R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.
- Obstetrical Society of Philadelphia.** (1868) *President*, Charles A. Behney. *Secretary*, John B. Montgomery, Pro tem, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.
- Chicago Gynecological Society.** (1878) *President*, William J. Dieckman. *Secretary*, Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.
- Brooklyn Gynecological Society.** (1890) *President*, James P. McManus. *Secretary*, William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.
- Baltimore Obstetrical and Gynecological Society.** (1929) *President*, Lawrence Wharton. *Secretary-Treasurer*, John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.
- Cincinnati Obstetrical Society.** *President*, Edward Friedman. *Secretary*, Carroll J. Fair, Cincinnati, Ohio. Third Thursday of each month.
- Louisville Obstetrical and Gynecological Society.** *President*, Layman A. Gray. *Secretary*, E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.
- Portland Society of Obstetrics and Gynecology.** *President*, Howard Stearns. *Secretary*, William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.
- Pittsburgh Obstetrical and Gynecological Society.** (1934) *President*, David B. Ludwig. *Secretary*, Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.
- Obstetrical Society of Boston.** (1861) *President*, Thos. Almy, Fall River, Mass. *Secretary*, Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.

*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the name is the year of founding.

- New England Obstetrical and Gynecological Society.** (1929) *President*, Frank A. Pemberton. *Secretary*, Fred. J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.
- Pacific Coast Obstetrical and Gynecological Society.** (1931) *President*, T. Floyd Bell. *Secretary-Treasurer*, William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.
- Washington Gynecological Society.** (1933) *President*, James R. Costello. *Secretary*, J. Keith Cromer, 1835 Eye St., N.W., Washington, D. C. Fourth Saturday, October to May.
- New Orleans Obstetrical and Gynecological Society.** (1924) *President*, E. L. Zander. *Secretary*, R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.
- St. Louis Gynecological Society.** (1924) *President*, S. A. Weintraub. *Secretary*, Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Meetings second Thursday, October, December, February, and April.
- San Francisco Gynecological Society.** (1929) *President*, R. Glenn Craig. *Secretary*, D. G. Morton, California University Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.
- Texas Association of Obstetricians and Gynecologists.** (1930) *President*, T. F. Bunkley. *Secretary*, J. McIver, 714 Medical Arts Bldg., Dallas, Tex.
- Michigan Society of Obstetricians and Gynecologists.** (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, Norman F. Miller. *Secretary*, Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).
- Obstetric Society of Syracuse Hospitals.** (1938) *President*, Edward C. Hughes. *Secretary*, Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May. Suspended for the duration.
- Alabama Association of Obstetricians and Gynecologists.** *President*, J. M. Weldon, Mobile, Ala. *Secretary*, Eva F. Dodge, Montgomery, Ala.
- San Antonio Obstetric Society.** *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.
- Seattle Gynecological Society.** (1941) *President*, R. Philip Smith. *Secretary*, Gerhard Ahnquist, 1336 Madison Street, Seattle. Meetings third Wednesday.
- Denver Obstetrical and Gynecological Society.** (1942) *Secretary*, Emmett A. Meehler, 1612 Tremont St., Denver, Colo. Suspended during war.
- Wisconsin Society of Obstetrics and Gynecology.** (1940) *President*, Roland S. Cron. *Secretary*, Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.
- San Diego Gynecological Society.** (1937) *President*, Geo. D. Huff. *Secretary*, Frank Russell, 233 A St., San Diego, Calif. Meetings held on the last Wednesday of each month.
- North Dakota Society of Obstetrics and Gynecology.** (1938) *President*, John D. Graham, Devil's Lake. *Secretary*, G. Wilson Hunter, 807 Broadway, Fargo, N. D.
- Virginia Obstetrical and Gynecological Society.** (1936) *President*, A. L. Carson, Jr. *Secretary*, L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.

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No. 2

Original Communications

PELVIC MODEL MANIKINS TO SHOW PELVIC SHAPE AND TO DEMONSTRATE LABOR MECHANISMS*

HOWARD C. MOLOY, M.D., M.S.C., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Columbia University and the Sloane Hospital for Women)

THE obstetrical manikin in its simplest form consists of an articulated pelvis and an artificial fetal head. The success of this method of teaching suggested the development of a series of models showing the classical and mixed inlet types previously described in detail,^{1, 2, 3} and the common variations in the mid and lower pelvis. It was considered mechanically possible to design each model for use as a manikin to demonstrate the influence exerted by pelvic shape upon head position and the common manual and forceps mechanisms. This objective has been obtained and the present presentation deals with the description, source of material and use of sixteen pelvic model manikins designed for teaching purposes.

Design and Use of Models

The series consists of sixteen models, fourteen showing pure and mixed pelvic types; one a male pelvis, and one an asymmetrical example.

Each model is made in a durable plastic material and is fixed to a solid metal base, supported by an adjustable U-shaped upright (Fig. 1). In this position, the student can inspect the pelvis and study its morphologic characteristics through the inlet, from the lateral aspect and through the subpubic arch. By adjustment of screws, A and B (Fig. 1) each model is converted into a fixed rigid manikin, Fig. 2.

The metal base is not essential if these models are kept permanently in a special manikin room. In this event the sixteen specimens can be displayed on a long table with the base support of the U-shaped

*This study has been made possible by a grant from the Commonwealth Fund.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

upright (Fig. 1C) permanently fixed to the table top. When it is necessary to use any model as a manikin the screws A and B (Fig. 1) are adjusted to bring the sacral tip to the edge of the table holding it rigidly as shown in Fig. 2.

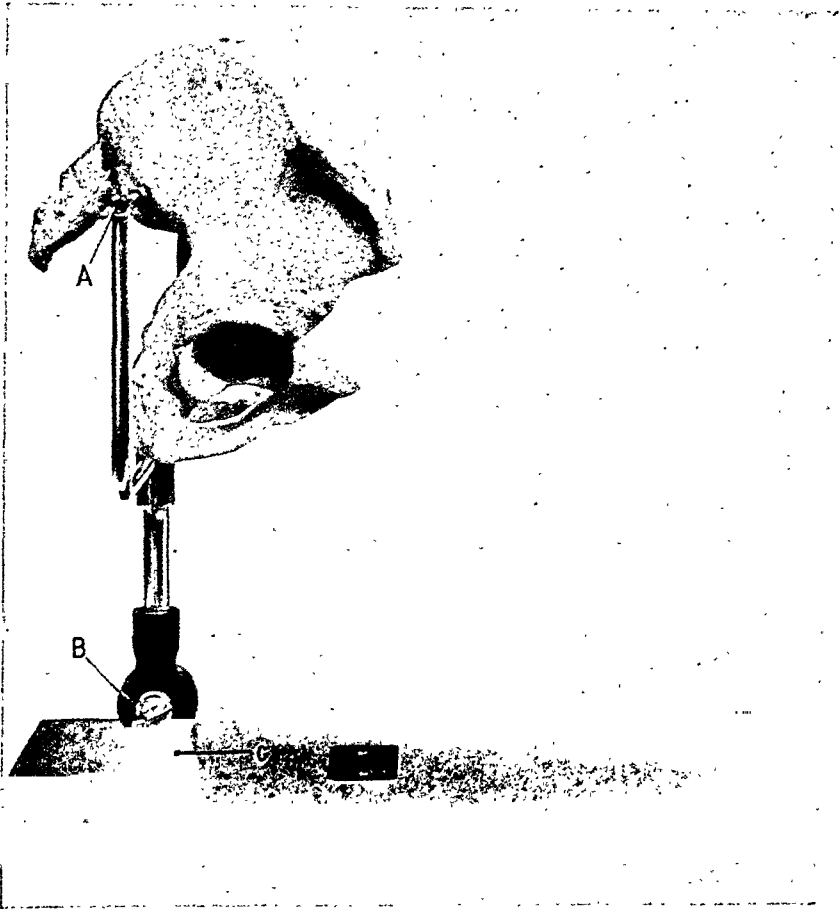


Fig. 1.—Model supported by U-shaped upright and fixed to a solid base in position for study of pelvic morphology. Screws A and B are adjustable. The metal base is not essential and joint C may be fixed permanently to any suitable manikin table.

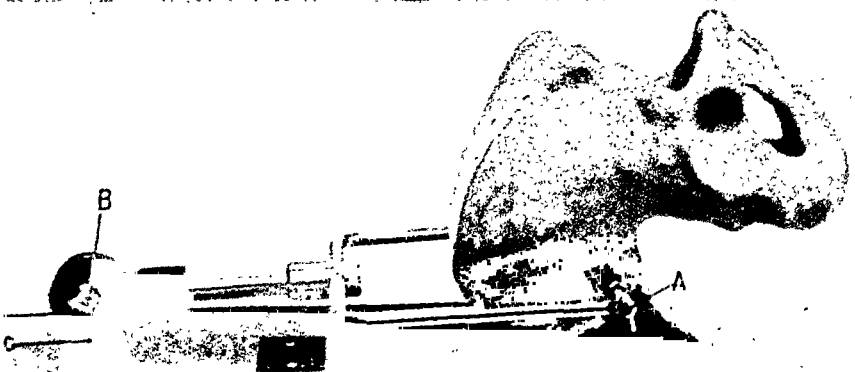


Fig. 2.—By adjustment of screw A and B, the pelvic model is converted into a rigid manikin.

Source of Material

The original pelves from which these models were constructed were selected from the well-known collection of the late Dr. T. Wingate Todd, Western Reserve University, Cleveland. This collection is unique in many ways. The sex of each skeleton is known, as well as the race and approximate age; also, in many instances, a brief medical history and photograph of the cadaver exists. Dr. Todd recorded the significant anthropometric measurements before maceration including the anteroposterior and transverse diameter of the inlet. The size of the collection is in itself important (over 800 female pelves) as it allows the observer greater choice of individual types.

Late in 1942, Dr. Normand Hoerr, head of the Department of Anatomy, Western Reserve University, became acquainted with this project and granted permission to visit his laboratory and examine, once again, the Todd skeletal material. Dr. W. W. Greulich, in the absence of Dr. Hoerr, extended every courtesy, demonstrated an interest in the grouping of these pelves according to type and approved the examples which were ultimately chosen for this series.

A Brief Description of Classification

The method of inlet classification used in the selection of these teaching models is diagrammatically illustrated in Fig. 3. In Fig. 3, A to D, the shape of the anterior and posterior segments of the four pure types is shown. Mixed forms are quite numerous and are classified according to the theory that mixed forms, in shape, appear to represent the fusion of a posterior segment of one pure type with an anterior segment of another pure form (Fig. 3, E to N). Theoretically, twelve mixed types occur, but the two anthropoid-flat combinations have not as yet been recognized. In the scheme of terminology for mixed types, the first term refers to the posterior segment and the second term to the anterior segment.

The pathologic types listed in the latest edition of Stander's revision of Williams' Textbook have been added to the morphologic classification under appropriate subdivisions.

Classification of Pelves*

I. NORMAL FEMALE GROWTH TYPES.

A. Variation at the inlet:

1. True anthropoid type.
2. Anthropoid-gynecoid type.
3. Anthropoid-android type.
4. True gynecoid type.
5. Gynecoid-anthropoid type.
6. Gynecoid-android type.
7. Gynecoid-flat type.
8. True android type.

*Published originally in *Gynecology and Obstetrics*, edited by Carl Henry Davis, M.D., W. F. Prior Co., Inc., Hagerstown, Md., T:Sec. III, Chapt. 15, pp. 82-83.

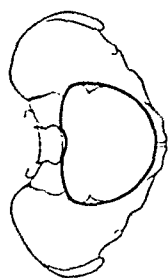
PURE TYPES

MIXED TYPES

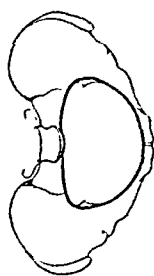
MIXED TYPES



J



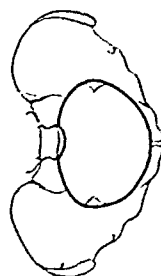
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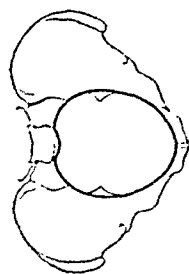
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E



F



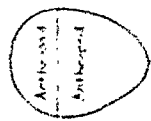
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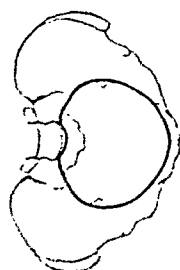
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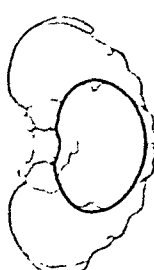
A



B



C



D

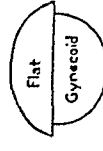
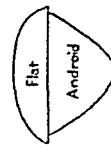
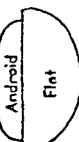
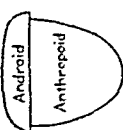


Fig. 3.—The principle of combining pelvic segments to classify the mixed inlet types. Pure types have a characteristic shape to the anterior and posterior segments (A-D). Mixed forms are classified by the combination of segments. The first term of a combination designates the posterior segment, the second term the anterior segment. A, Pure gyneco-android; B, pure gyneco-android; C, pure gyneco-android; D, pure gyneco-android; E, gyneco-android (mixed); F, gyneco-android (mixed); G, gyneco-android (mixed); H, gyneco-android (mixed); I, gyneco-android (mixed); J, gyneco-android (mixed); K, gyneco-android (mixed); L, gyneco-android (mixed); M, gyneco-android (mixed); N, gyneco-android (mixed).

9. Android-anthropoid type.
10. Android-gynecoid type.
11. Android-flat type.
12. True platypelloid type.
13. Flat-gynecoid type.
14. Flat-android type.

B. Variations below the inlet:

1. Side walls of pelvis-----divergent, straight, or convergent.
2. Subpubic arch -----wide, moderate, narrow.
3. Pubic rami -----straight (masculine or Gothic),
curved (feminine or Norman).
4. Pubic symphysis -----masculine or feminine type.
5. Ischial spines -----long, sharp, short, or flat.
6. Apex of sacrosciatic notch-----wide, average, narrow.
7. Base of sacrosciatic notch-----wide, average, narrow.
8. Number of sacral segments.
9. Sacral curvature -----(a) longitudinal—straight, average,
marked.
(b) transverse—straight, average,
marked.
10. Sacral inclination -----(a) upper portion—forward, average,
backward.
(b) lower portion—forward, average,
backward.
11. Terminal sacrum -----sharp, average, blunt.
12. Lateral bore -----divergent, straight, convergent.

C. General pelvic variations:

1. Pelvic size -----(a) large, average, small.
(b) pelvimetry measurements of cardinal diameters.
2. Pelvic bones -----heavy, average, light.
3. Symmetry of pelvis----- (a) symmetrical at inlet, mid, or lower pelvis.
(b) asymmetrical (to right) at inlet, mid or lower pelvis.
(c) asymmetrical (to left) at inlet, mid, or lower pelvis.

II. ABNORMAL GROWTH AND DEVELOPMENTAL TYPES.

(In addition to the abnormality, the pelvis may be classified morphologically as outlined in Group I.)

1. Infantile.
2. Dwarf.

III. TYPES CAUSED BY DISEASE OF THE PELVIC BONES AND JOINTS.

(In addition to the abnormality, the pelvis may be classified morphologically as outlined in Group I.)

A. Metabolic:

1. Rachitic:
 - a. Flat.
 - b. Generally contracted and flat.
 - c. Generally contracted.
2. Osteomalacic.

B. Congenital, inflammatory, and atypical types:

1. Assimilation pelvis.
2. Split pelvis.
3. Naegele's pelvis.
4. Robert's pelvis.
5. Coxalgic.
6. Coxarthrolisthetic.
7. Pelvis spinosa.
8. Neoplastic.

C. Traumatic types:

1. Fracture of pelvis.
2. Separation of symphysis.

PELVIC INDEX

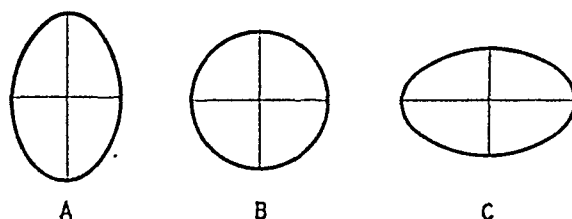


Fig. 4.—The pelvic index reveals a transition in shape from a longitudinal ellipse through a round form to a transverse ellipse, A, B, C.

IV. TYPES SECONDARY TO ABNORMALITIES IN THE SPINAL COLUMN.

(In addition to the abnormality, the pelvis may be classified morphologically as outlined in Group I.)

1. Kyphotic pelvis.
2. Kyphorachitic pelvis.
3. Scoliotic pelvis.
4. Kyphoscoliotic pelvis.
5. Kyphoscoliorachitic pelvis.
6. Spondylolisthetic pelvis.

V. TYPES SECONDARY TO ABNORMALITIES OF THE LOWER EXTREMITIES.

(In addition to the abnormality, the pelvis may be classified morphologically as outlined in Group I.)

1. Luxation of femora.
2. Atrophy or loss of one or both extremities.

A careful study will show that there are at least five factors to consider in devising a classification of pelves sufficiently comprehensive to describe the pelvis as a whole from inlet to outlet.

First.—The classification must take into account the so-called pelvic index which concerns the relationship of the length of the anteroposterior diameter of the inlet to the widest transverse diameter of the inlet. This index reveals a transition in shape from the extreme long narrow oval through the round to the flat or transverse oval shape.

(Fig. 4.) This transition in shape may be demonstrated in the pelvic models if the observer studies the inlet views of the following types in series: anthropoid-android, anthropoid, anthropoid-gynecoid, gynecoid-anthropoid, gynecoid, gynecoid-flat, flat-gynecoid and the typical platypelloid type. Individual pelves in the above series may show variations not indicated by the pelvic index. This observation introduces the second and third factors to consider in this classification.

Second.—There is individual variation in the shape of the posterior segment of the inlet. The widest transverse diameter divides the pelvis into an anterior and posterior segment and the point of intersection of this diameter with the anteroposterior diameter forms the anterior and posterior sagittal diameter at the inlet. Variations in the position of the widest transverse diameter effects equal variations in the lengths of these inlet sagittal diameters. Four characteristic types of posterior segments can be recognized and are illustrated diagrammatically in Fig. 5. These are the posterior segments of the “anthropoid,” “gynecoid,” “android,” and “platypelloid” pelvic types. It may be pointed out that there are intermediate forms of posterior segments between the four classical shapes illustrated in Fig. 5. Experience has shown that these four posterior segment shapes are quite adequate for classification purposes.

FOUR CLASSICAL POSTERIOR SEGMENTS

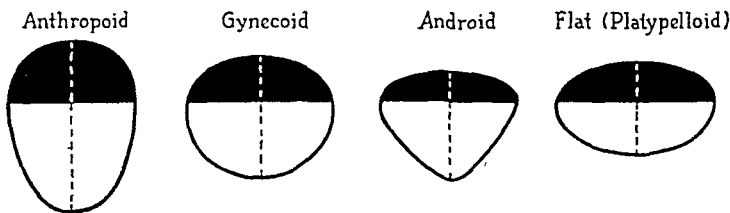


Fig. 5.—The pelvic index does not consider the relationship of the widest transverse diameter of the inlet to the anteroposterior diameter. In the classic or pure types the point of intersection produces variable posterior and anterior sagittal diameters with a typical posterior segment for each type.

Third.—This factor deals with the variations in the anterior segment. The four classical or pure pelvic types of course, possess characteristic anterior segments which are termed “anthropoid,” “gynecoid,” “android,” and “flat” (platypelloid). (Fig. 6.) Intermediate shapes between those classical types also occur in the anterior segment, and their classification may afford difficulty to the inexperienced observer unless the trend in forepelvic variations is understood. The factors which modify the shape of the anterior segment at the inlet appear to resemble in overlapping of sexual characteristics (Fig. 6A). Female characters produce a well-formed wide anterior segment with good curvature to the iliopectineal lines radiating from the symphysis. (Fig. 6B.) Male characters produce a narrow angular anterior segment with straight iliopectineal lines deviating backward from the symphysis. (Fig. 6C.) Lack of curvature in the side walls of the anterior segment at the inlet is considered in itself, a masculine character and gives a characteristic angular or wedge-shaped appearance without regard to the size of the retropubic angle. Thus an “android” anterior segment may be “narrow,” “average,” or “wide,” providing the lateral borders are straight enough to produce an angular shape. (Fig. 6C.) This explains

why the term "flat android" is used to designate a flat pelvis with a blunt wedge-shaped appearance, or why the term "anthropoid-android" is used to define an anthropoid pelvis with a narrow forepelvis. If the forepelvis has a long anterior sagittal diameter, it may be termed "anthropoid," as is used in the "android-anthropoid" type.

The anthropoid, gynecoid and flat anterior segments, in classical types, are well formed and female in shape (Fig. 6A) and the differences in these types concern chiefly the size of the retropubic angle and, to a lesser extent, the length of the anterior sagittal diameter. Steele and Javert⁴ have recently described the "anterior transverse diameter" through the forepelvis which, when compared to the widest transverse diameter, gives a linear expression of the curvature present in the forepelvis which is an aid in the recognition of the android anterior segment.

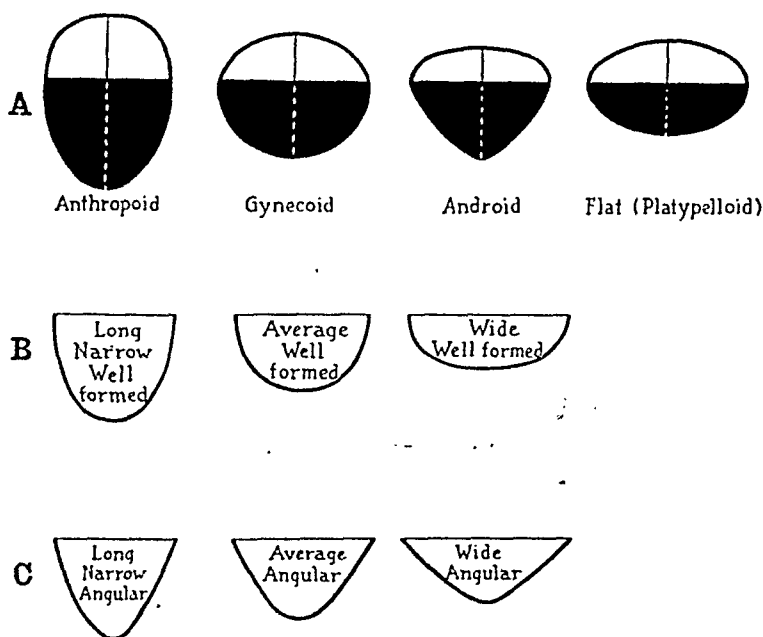


Fig. 6.—Factors affecting shape in the anterior segment. A, The classical shape for the anthropoid, gynecoid, android, and flat anterior segments; B, the appearance of female characteristics associated with narrow, moderate, and wide retropubic angles; C, the appearance of male characteristics associated with narrow, moderate, and wide retropubic angles.

Fourth.—Variations in the side walls, sacral curvatures and inclinations, size and shape of the subpubic arch, number of sacral segments and other features must be expressed by an appropriate terminology. A complete list of terms is outlined in the formal classification.

Fifth.—There are a number of variable factors that affect the pelvis as a whole and these, including the lengths of the cardinal pelvic diameters, are listed in the formal classification.

Selection of Typical Types for Teaching Models

From the information listed in the history associated with each skeleton in Todd's collection, it is possible to divide the pelvises into two racial groups—white and Negro. It is admitted, however, that the American Negro is no longer a pure racial type. The white race also shows great racial intermixture. In the work associated with the selection of suitable pelvic types, two long tables were used—one for

the white group and one for the so-called Negro group. Each individual pelvis was classified according to the principles outlined in the formal classification. Slowly, as more pelves were examined and classified, fourteen collections of pelves accumulated on each table, totaling approximately three hundred pelves.

During the process of typing this large series of skeletal pelves, several interesting observations were made. It was noted that in pelves which demonstrated marked convergence of the side walls, the inlet usually revealed a long oval or anthropoid tendency. A number of excellent android types were found with a characteristic wedge-shaped inlet but, as a rule these examples showed straight side walls with an ample subpubic arch or some other variations from the classical android form. The pelves showing a characteristic masculine posterior segment, frequently revealed a forepelvis which was too well formed to select as a typical android type. This fact is noted in the excellent android-gynecoid type finally chosen for the teaching series (Fig. 7K). For these reasons, the android example which was selected to show convergence of the side walls and a narrow subpubic arch, has a longer anteroposterior diameter than is found in the classical or pure android type. The selected example (Fig. 7C), therefore, does not appear to show the characteristic flat posterior segment of a typical android. Careful examination of this specimen reveals that the apparently ample appearance of this posterior segment is caused by the transverse or coronal curvature in the first sacral segment. The notch is quite masculine at the apex and the section of the ilium over the apex of the notch is characteristically short.

Difficulty was encountered in the classification of the mixed anthropoid-gynecoid types and the gynecoid-flat forms. Many mixed anthropoid types, i.e., gynecoid-anthropoid and anthropoid-gynecoid types, were found and it was difficult to determine whether certain individual pelves belonged in one or the other mixed group. The key-diagram shown in Fig. 3, is a great aid in the classification of these doubtful examples. Individual observers might disagree in the typing of these indeterminate types but an error in typing is not serious as long as the pelvis is recognized as of a shape intermediate between the classical anthropoid and gynecoid forms. The same difficulty was found in the classification of "gynecoid-flat," and "flat-gynecoid" combinations. Here again, if attention is paid to the position of the widest transverse diameter and its point of intersection on the anteroposterior diameter, these mixed flat types can be classified into their correct group without too much difficulty.

This discussion of the practical difficulties encountered in selecting a series of skeletal pelves from which to make a set of teaching models illustrates that individual pelves show many minor characteristics which either cannot be classified or which detract from the classical

prototype. Of course this observation is not unexpected when dealing with anatomic material. A teaching series of models could be developed by a good sculptor, who understood the anatomic significance of the shapes of the prototypes illustrated in Fig. 3. It would be quite possible for him to add the common variations in the mid and lower pelvis which are outlined in the formal classification. However, after granting this possibility, it is felt that models made from actual skeletal material, have greater value for teaching purposes, because they show the combination of variations which can be expected in living patients.

The frequency of occurrence of the fourteen pelvic types, for each race is of interest. The same trend indicated in Table I was also noted in our original study of this same material in 1933, at which time, the pelvis were classified into the four classical types, i.e., anthropoid, gynecoid, android and platypelloid.

TABLE I. FREQUENCY OF OCCURRENCE

| | WHITE RACE | | NEGRO RACE | |
|---------------------|------------|----------|------------|----------|
| | NUMBER | PER CENT | NUMBER | PER CENT |
| Anthropoid | 6 | 5 | 14 | 8.1 |
| Anthropoid-gynecoid | 7 | 5.8 | 21 | 12.2 |
| Gynecoid-anthropoid | 6 | 5 | 27 | 15.7 |
| Anthropoid-android | 6 | 5 | 7 | 4.1 |
| Android-anthropoid | 3 | 2.5 | 2 | 1.2 |
| Android | 4 | 3.3 | 5 | 3 |
| Gynecoid-android | 13 | 10.8 | 22 | 12.9 |
| Android-gynecoid | 6 | 5 | 7 | 4.1 |
| Gynecoid-flat | 3 | 2.5 | 1 | 0.6 |
| Flat-gynecoid | 4 | 3.3 | 1 | 0.6 |
| Android-flat | 3 | 2.5 | 1 | 0.6 |
| Flat-android | 2 | 1.6 | 3 | 1.7 |
| Flat | 2 | 1.6 | 1 | 0.6 |
| Gynecoid | 55 | 45.8 | 60 | 34.9 |
| Total | 120 | | 172 | |

The Negro race shows a higher incidence of anthropoid and anthropoid-mixed types. The white race shows a slightly higher incidence of flat, mixed-flat, and android types than the Negro race.

Description of Pelvic Models

The Anthropoid-Android Type.—Fig. 7F (Prototype Fig. 3F). Western Reserve No. 3210, Negro.

This is an unusually fine example of an anthropoid-android type. The long narrow anterior segment gives to the pelvic inlet a more extreme long oval appearance than is noted in the classical anthropoid type. This particular example is ideal to use in demonstrating the extreme anthropoid characters and the classical posterior mechanism which is common to the anthropoid and related mixed types.

The narrow forepelvis increases the possibility of a posterior mechanism because the narrow anterior segment receives the frontal region of the head more readily than the rounded occiput. For this reason the anthropoid type with a narrow forepelvis should be distinguished from the typical anthropoid pelvis with a well-formed forepelvis in which an-

terior oblique positions occur more frequently than posterior positions. Hence, this particular mixed type is correctly classified as an "anthropoid-android" mixed form.

The Anthropoid Type. Fig. 7A (Prototype Fig. 3A). Western Reserve No. 2172, Negro.

In order to emphasize the characters of the anthropoid-android type just described, it is necessary, for contrast, to select the classical anthropoid example to show a well-formed long narrow oval shape. Certain observers may contend that this particular example is too gynecoid in appearance to represent the classical anthropoid form, and may consider it more characteristic of a gynecoid-anthropoid or anthropoid-gynecoid mixed type. However, to select a narrower long oval than the example shown, would tend to place the pelvis in the anthropoid-android group. The actual specimen shows more anthropoid characters than is indicated in the photograph of the model as shown in Fig. 7A.

Anthropoid-Gynecoid Type.—Fig. 7E (Prototype Fig. 3E). Western Reserve No. 2116, Negro.

This type and the gynecoid-anthropoid mixed form are quite similar in general inlet shape. The classical differences are indicated to better advantage in the prototypes Fig. 3 E and G. The chief differences exist in the position of the widest transverse diameter and the point of intersection on the anteroposterior diameter. The anthropoid-gynecoid type has a very wide sacrosciatic notch with a very long segment of ilium over the apex of the notch between the point of origin of the widest transverse diameter and the sacroiliac synchondrosis. This feature may be emphasized by the presence of a transverse sacral curvature in the first sacral segment.

Gynecoid-Anthropoid Type.—Fig. 7G (Prototype Fig. 3G). Western Reserve No. 715, White.

In this example the posterior segment has a flat appearance because the sacrosciatic notch is not so wide as in the anthropoid-gynecoid type and the section of ilium at the apex of the notch is not as long. The anthropoid appearance may result from slight narrowing of the retro-pubic angle of the anterior segment behind the symphysis. This particular example was also selected to show a markedly forward lower sacrum with six sacral segments.

Gynecoid Type.—Fig. 7B (Prototype Fig. 3B). Western Reserve No. 2337, White.

In skeletal material, as well as in roentgenologic examinations, excellent examples of all types are seen. When it comes to the problem of selecting one good example of the type, minor deviations from the classic prototype are prone to exist. The specimen selected to reveal the characteristic gynecoid features is a fairly representative specimen. The shape of the inlet is quite characteristic. The ischial spines, however, are slightly more prominent than occurs in the classical gynecoid. This specimen was selected because the inlet, sacrosciatic notch and sub-pubic arch conform to the classical gynecoid prototype.

The Gynecoid-Flat (Mixed) Type.—Fig. 7I (Prototype Fig. 3I). Western Reserve No. 415, White.

This type in general appearance is quite similar to the flat-gynecoid type Fig. 7N. The chief difference between these types is shown in the

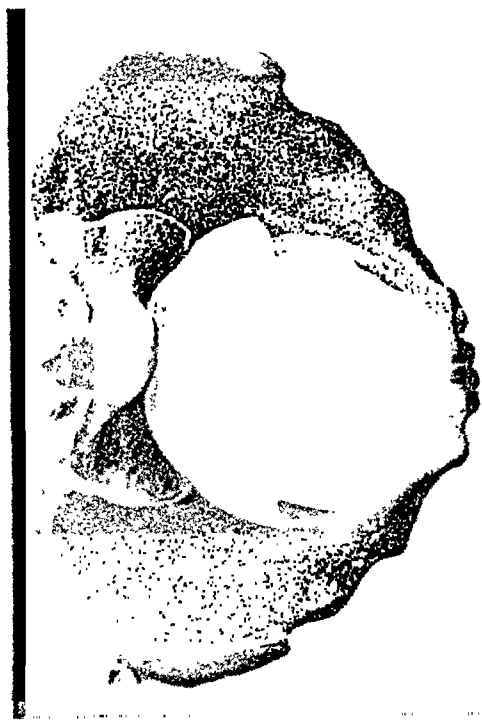
(Text description, continued on p. 168.)



Figs. 7A-P.—Inlet, lateral and subpubic arch views of models. A, Pure gynecoid type. W. R. 2172; B, pure gynecoid type. W. R. 2337; C, pure gynecoid type. W. R. 1256; D, pure gynecoid type. W. R. 3210; E, gynecoid-gynecoid (mixed) type. W. R. 715; F, gynecoid-gynecoid (mixed) type. W. R. 2116; G, gynecoid-gynecoid (mixed) type. W. R. 2476; H, gynecoid-gynecoid (mixed) type. W. R. 603; I, gynecoid-gynecoid (mixed) type. W. R. 1924; J, gynecoid-gynecoid (mixed) type. W. R. 2708; K, gynecoid-gynecoid (mixed) type. W. R. 2860; L, gynecoid-gynecoid (mixed) type. W. R. 111.



Fig. 7.—C, Pure android type, W. R. 1256; D, pure platypelloid type, W. R. 1208.



E.



E.



FIG. 7.—E. Anthropoid-Eynecoid (mixed) type, W. R. 2116; F, anthropoid-android (mixed) type, W. R. 3210.



G.



H.



Fig 7.—G, Gynecoid-anthropoid (mixed) type, W. R. 715, H, gynecoid-android (mixed) type, W. R. 2476.



Fig. 1.—4, Gynecoid-flat (mixed) type, W. R. 415; J, android-anthropoid (mixed) type, W. R. 2708.



Fig. 7.—K, Android-gynecoid (mixed) type, W. R. 603; L, android-flat (mixed) type, W. R. 454.

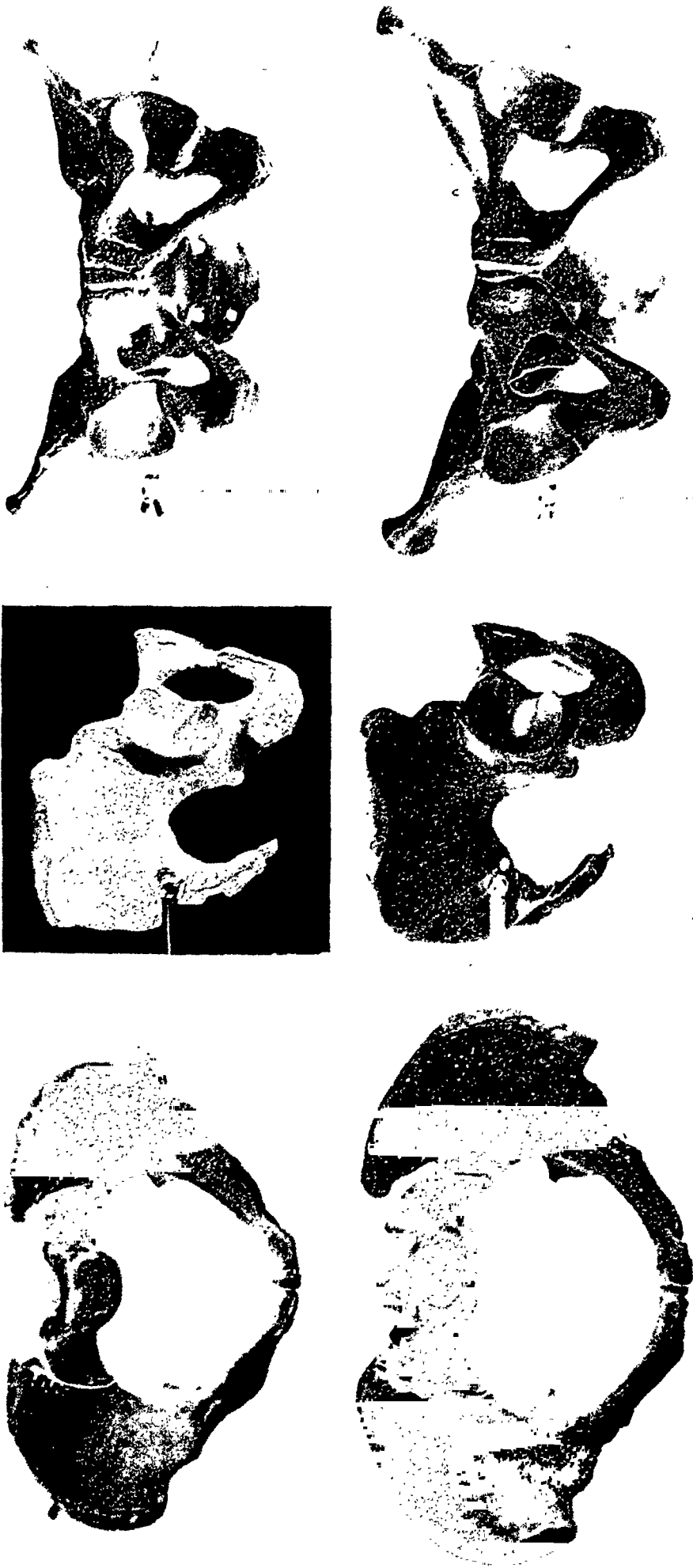


Fig. 7.—M, Flat-android (mixed) type, W. R. 1924; N, flat-gynecoid (mixed) type, W. R. 2860.



Fig. 7.—O, Male pelvis. Department of Anatomy, College of Physicians and Surgeons; P, asymmetrical pelvis, W. R. 111.

position of the widest transverse diameter. In the gynecoid-flat type, the widest transverse diameter is placed forward on the anteroposterior diameter, the sacrosciatic notch is wide and the section of ilium over the apex of the notch, between the origin of the widest transverse diameter and the sacroiliac synchondrosis is ample. The sacrum has a marked concavity with a forward sacral tip and six segments.

Flat-Gynecoid Type (Mixed).—Fig. 7N. (Prototype Fig. 3N). Western Reserve No. 2860, White.

This type has a more flattened appearance than the gynecoid-flat. The posterior segment is flat because the widest transverse diameter is closer to the sacrum. This feature causes a narrower sacrosciatic notch.

True Platypelloid Type (Pure).—Fig. 7D (Prototype Fig. 3D). Western Reserve No. 1208, Negro.

This example shows the characteristic features of a pure flat type. The inlet, a transverse flat oval is well formed and the widest transverse diameter tends to favor the midcoronal axis of the pelvis. The specimen is a small example of the classical type.

True Android Type (Pure).—Fig. 7C (Prototype Fig. 3C). Western Reserve No. 1256, White.

The prototype calls for a wedge-shaped inlet caused by a flat posterior segment and a narrow forepelvis with straight iliopectineal lines radiating from the symphysis. At lower levels the side walls converge to a narrow subpubic arch, and the lateral view shows a narrow, masculine sacrosciatic notch with a forward sacrum. The example selected does not reveal all these classical features. It will be noted that the posterior segment is not so characteristically masculine as the prototype demands, and the inlet has an elongated appearance. This particular example was selected because it shows the marked side-wall convergence and a narrow subpubic arch which represent typical masculine characters. The lower sacrum has a forward inclination. It is the transverse sacral concavity which detracts from the typical masculine appearance of the posterior segment at the inlet in this particular example.

Android-Gynecoid Type (Mixed).—Fig. 7K (Prototype Fig. 3K). Western Reserve No. 603, White.

This is an unusually fine example. The posterior segment is very masculine in appearance. The sacrosciatic notch is narrow. The anterior segment is well formed and gynecoid in appearance. The combined segments give a slightly flat effect. The sacrum has six segments and is straight with an average to backward inclination.

Gynecoid-Android Type (Mixed).—Fig. 7H (Prototype Fig. 3H). Western Reserve No. 2476, Negro.

This is a gynecoid or normal pelvis with a narrow anterior segment. Upon casual study of the posterior segment, it might be supposed that the segment is not characteristically gynecoid. It appears to present a flat shape. This fact is due in part to the presence of an overhanging sacral promontory associated with a backward inclination to the sacrum. The specimen was selected to show this particular type of sacral variation. However, if the shape of the posterior segment is viewed at the plane of the inlet, where the iliopectineal lines, if continued, would cross the anterior surface of the first sacral segment, the gynecoid characters of the posterior segment will be evident. The masculine character of the forepelvis expressed by a narrow angle behind the symphysis is also present.

Android-Anthropoid Type (Mixed).—Fig. 7J (Prototype Fig. 3J). Western Reserve No. 2708.

The prototype calls for a flat posterior segment and a long narrow anterior segment, thereby producing an elongated anthropoid appearance (Fig. 3J). The specimen selected demonstrates these features satisfactorily. More characteristic examples have been recognized especially in roentgenograms of living women. The posterior segment in the illustrated example is not quite as flat or masculine in appearance as in the prototype. However, this particular specimen shows an excellent example of a straight sacrum and the inlet appearance is made characteristic by a narrow anterior segment associated with convergence of the side walls at lower levels.

Flat Android Type (Mixed).—Fig. 7M (Prototype Fig. 3M). Western Reserve No. 1924, Negro.

This is an excellent example. Although the angle of the anterior segment is wide, the iliopectineal lines are straight and this feature, in conjunction with the flat posterior segment, gives a flat wedge-shaped angular appearance to the pelvic inlet. This particular specimen is a small example of the prototype, and it is doubtful if it would be adequate for delivery of a child of average size. Certain examples of this type show convergence of the side walls at a lower level.

Android Flat Type (Mixed).—Fig. 7L (Prototype Fig. 3L). Western Reserve No. 454, White.

This type is difficult to distinguish from the flat-gynecoid type. The widest transverse is close to the promontory and the iliopectineal lines curve acutely inward toward the sacroiliac synchondrosis over the apex of the sacrosciatic notch. As a result, the posterior segment has a flatter posterior segment than occurs in the flat gynecoid. The anterior segment is wider and the anterior sagittal diameter is usually shorter than in the flat gynecoid type. The straight sacrum has a slightly backward inclination.

Typical Masculine Pelvis.—Fig. 70, College of Physicians and Surgeons, Dept. of Anatomy.

This fine example of a male pelvis needs no comment. It was selected to show all the characteristic male features which have been described, i.e., heavy bones, narrow Gothic subpubic arch, male symphysis, converging side walls, narrow sacrosciatic notch and a characteristic wedge-shaped inlet.

Common Asymmetrical Type.—Fig. 7P, Western Reserve No. 111, White.

This example was included in the teaching series for general anatomic interest. Slight asymmetry is common in occurrence. In a series of 215 complete roentgenologic examinations in living women, pelvic asymmetry was observed in 4 per cent of the cases.

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HERPES GESTATIONIS*

With a Report of Two Cases and a Survey of the Literature

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HERPES gestationis is an uncommon cutaneous complication of pregnancy, being a chronic polymorphous exanthema characterized by recurrent crops of grouped bullae and vesicles on erythematous bases and associated with severe pruritus.

Ormsby and Montgomery³⁴ definite herpes gestationis as being a variety of dermatitis herpetiformis, differing from that disease only in its exciting cause—pregnancy. Accordingly, one may expect in this syndrome a considerable degree of variability as to the time of onset, signs, symptoms, and response to therapy.

First described by Bunel³¹ in 1811, the condition has been variously referred to as dermatitis multiformis gestationis, herpes circinatus bullosus, hydroa gravidarum, hydroa herpetiformis, pemphigus pruriginosus, and prurigo gestationis. The generally accepted term “herpes gestationis” was first suggested by Milton¹ in 1872.

Comprehensive summaries of the literature have been previously recorded by Duhring,² Tommasi,⁶ and Howard.¹³

Although its incidence is not very great, the disease is probably more common than one would be led to believe from the number of cases reported in the obstetric literature. Irving¹⁹ has stated that no patients with this dermatosis had been admitted to the Boston Lying-in Hospital in a recent 20-year period. Turner and Zakon²⁰ through personal communications found that many obstetricians had never encountered the disease. In a review of the American literature for the past 10 years, we have been able to collect references to 15 cases of herpes gestationis and mention of 18 others. To this group, we add two additional cases, making a total of 35 cases in all.

Etiology

The etiology of the disease is unknown. Many authors feel that the cutaneous lesions result from injury to the vasomotor nerves by toxins or ferments manufactured by the fetal tissues or by cells of the chorionic epithelium. These substances may ordinarily be neutralized by anti-ferments or as seems more plausible, are formed only in quantity when the chorionic villi disintegrate. Inasmuch as placentas of even normal women with no demonstrable organic disease are prone to show areas of

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infarction, dissolution of tissue at the time of such accidents may well explain the periodic exacerbations of the disease.¹³

Several investigators have advanced the theory that renal insufficiency accounts for the appearance of the disease. Perrin³ found urea, total nitrogen, and chloride retention. Presumably, there would be an accompanying failure to eliminate toxins or similar bodies of high molecular weight.

Sayer²⁶ felt that the disease represents a toxic disturbance induced by impaired hepatic function. In his opinion, the liver is unable to cope with the added burden of fetal metabolism and fails to function in its usual role of detoxification. Del Vivo¹⁰ also noted hypofunction of the liver as determined by laboratory examinations in a case which he observed. Sechi¹² found a normal liver function test on his patient.

Del Vivo, however, advocated the theory that the disease represents an anaphylactic mechanism resulting from sensibilization to certain antigens as yet unknown, and which may differ from time to time. His patient presented a cutaneous hypersensitivity to globulins and albumins from her own placenta. Sulzberger and Rostenberg¹⁷ pointed out that the nature of the presumptive allergens is, as yet, unknown, and routine cutaneous testing is therefore impossible. Werther⁷ likewise expressed the belief that the cutaneous manifestations in herpes gestationis were an allergic phenomenon. Crosti's patient showed no cutaneous allergic reactivity to follicular, lutein, or placental preparations, but injections of these substances were capable of causing significant reacutizations of the objective and subjective symptoms.¹¹

A few investigators have considered an endocrine disturbance to be a factor of prime importance in the etiology. Tommasi⁶ suggested that the disease resulted from ovarian hypofunction. Sechi¹² in 1932 employed corpus luteum hormone in the treatment of a case of herpes gestationis and noted immediate regression of the eruption. An acute exacerbation immediately post partum was likewise controlled. He concluded, therefore, that herpes gestationis was due to a disturbance in the production of corpus luteum hormone. Gilman¹⁵ in 1933 reported similar success. Kampf²⁷ in 1940 noted that corpus luteum extracts seemed to lessen the pruritus of the disease and to cause the eruption to slowly regress.

Rostenberg²⁸ noted, in his patient, that the gonadotropin was protracted for several months after parturition. Weidman²¹ observed that the degree of pruritus varied with fluctuations in the gonadotropic principle, there being a greater quantity in those with mild pruritus and a lesser in those with severe pruritus.

Elliott²⁰ in 1938 reported a case of skin rash occurring in association with choriocarcinoma secondary to a hydatidiform mole. Inasmuch as the cutaneous manifestations appeared about the time the chorioma appeared to grow, and inasmuch as they became more extensive with increased activity of this malignant growth, he concluded that the skin rash should be classified as herpes gestationis. He suggested that the Aschheim-Zondek test might be positive in high dilutions in cases of herpes gestationis during pregnancy, and that this titer might remain high even post partum when an acute exacerbation of the disease was noted following delivery. The Aschheim-Zondek test is said to be usually negative by the seventh post-partum day. A Friedman modification of the Aschheim-Zondek test was performed on one of our patients

on the tenth post-partum day, and this was negative despite a severe exacerbation of her dermatitis at that time.

Antoine⁹ ascribed the disease to a toxicosis produced by the ovum in association with an unknown virus.

In many cases reported in the literature, herpes gestationis occurred only in pregnancies terminating in the birth of infants of the same sex.²³ Lewis²² reported a case in which the woman developed herpes gestationis during two previous pregnancies, and each time the offspring proved to be a male. On a third occasion she delivered a female, and no symptoms of the disease were noted throughout her pregnancy. On a fourth pregnancy, however, the disease again appeared; and as was prognosticated, a male was later delivered. This hypothesis was refuted by Costello in 1941, when he reported two successive pregnancies in the same patient, severely complicated by herpes gestationis, the first time a boy being delivered, the second time a girl.

Signs and Symptoms

Although the disease may appear at any time during pregnancy, it is more common to the latter half of gestation. It rarely appears before the fourth month of pregnancy. The disease seems to be more frequent in primiparous and uniparous patients. The greatest number of cases have been reported in the age group of 30 to 35 years. The disease may recur with monotonous regularity in each of many successive gestations, or return intermittently every second or third pregnancy.¹³

The onset of the disease is marked by a severe generalized burning sensation succeeded by a pruritus. Then a patchy erythema develops on the extremities, occasionally on the trunk. During the next 24 hours, these erythematous patches enlarge and herpetiform crops of small vesicles appear. In some areas, the vesicles are noted to surround a red macule or a slightly raised and edematous plaque, either at its junction with normal skin or aligned on a palpably elevated margin. The vesicles soon coalesce to form tense, thick-walled bullae of assorted sizes. A few of the bullae subsequently appear to arise from apparently normal skin. Upon rupture of the bullae, the serous crusts eventually fall away, leaving as a rule only a brownish pigmentation. Mucosal lesions are rare but do occur.

The pruritus associated with the disease is intense and persistent; and in the early stages is disproportionately in excess of the amount of the eruption. Excoriations of the skin are not prominent, however, even though the patient generally indulges in considerable scratching. This is due to the fact that the lesions do not readily rupture, and that they tend to refill immediately after being evacuated.

Once the disease appears, it usually progresses to the termination of gestation, showing many cyclic flare-ups and remissions. The exacerbations are usually accompanied by mild to severe constitutional symptoms of albuminuria, dyspnea, dyspepsia, fever, malaise, and neuralgic pains. Eosinophilia during the acute exacerbation may range as high as 50 per cent. During the first few days post partum, a final acute exacerba-

tion is usually followed by a permanent regression of all signs within two weeks to three months. Occasionally, following delivery, episodes of severe pruritus and burning precede the onset of the first few menstrual periods. Infrequently, a bullous or vesicular eruption may appear. Such flare-ups are termed herpes menstrualis recidivans.

Differential Diagnosis

The diagnosis of herpes gestationis must be differentiated at times from other toxic dermatoses such as drug eruptions, erythema multiforme bullosum, impetigo herpetiformis, and pemphigus. The latter two are usually fatal. In many cases, the diagnosis will be contested, even amongst dermatologists, pending final outcome of the illness.

Prognosis

The prognosis for the mother is fairly good, although a few cases with fatal outcome have been reported. The prognosis seems worse, the earlier in pregnancy the disease appears. The disease is likely to occur earlier and to be of increasing severity in succeeding pregnancies.²⁴

The prognosis for the child is much less hopeful. The incidence of spontaneous abortions, monstrosities and stillbirths is high among women afflicted with herpes gestationis or predisposed to it. Costello²³ reported his case in which the woman delivered a normal child with her first pregnancy, and an anencephalic infant with spina bifida with the second. Isbister⁸ reported a case in which the first born, a 6¼-pound infant died on the fourth day after delivery without obvious reasons. In the second pregnancy, the same patient delivered a stillborn infant. In del Vivo's case, a second pregnancy terminated in the delivery of a premature infant with bilateral microphthalmus and a cleft palate.

Nevertheless, a number of normal infants have been obtained at term. Infants delivered of mothers afflicted with herpes gestationis must be guarded against intercurrent infections during the first year of life.

Cutaneous lesions may occur in the child, but this apparently has little to do with the prognosis. Tommasi⁸ reported two cases in which lesions of the skin developed on the infants after birth, but disappeared within a few days, leaving no evidence of their former presence. Milton¹ reported a case presenting an alternation of stillbirths and live babies, demonstrating cutaneous lesions in both the healthy and dead children. Furthermore, one from the group of dead children showed no evidence whatever of an abnormality of the skin.

Therapy

The treatment for herpes gestationis is not too efficacious, and the course of the disease in the majority of cases seems little influenced by the therapy. The prevention of secondary infection and general supportive measures are the most important. Locally, aqueous astringent

baths, abscission of the larger bullae, and topical applications of anti-septic lotions are advised. Irradiation of local lesions sometimes affords relief.

Heiman²⁹ suggested the intravenous injection of 10 c.c. of a 10 per cent solution of strontium bromide to afford relief from the generalized pruritus.

Fowler's solution has been suggested as therapy, and in some cases has been highly effective. It is best given in full therapeutic dosage, and still better if administered in intermittent courses.

Eichmann⁴ reported one case in which cure was obtained by daily 300 c.c. infusions of Ringer's solution, intended to change the mineralization and ion concentration of the blood.

In some cases, autohemotherapy, serum from normal pregnant women especially if of the same stage of gestation, or injections of horse serum have been effective. Ormsby reported excellent results in one case, administering 20 c.c. intramuscularly at 5-day intervals of the blood serum obtained from another normally pregnant female. On the other hand, Britzman⁵ had only partial success with human serum, but reported a permanent cure by the intramuscular injection of boiled milk.

Tommasi⁶ reported two cases in which ovarian extract was administered with eventual success. Turner and Zakon³⁰ gave their patient 600,000 units of progynon B and 70 milligrams of proluton over a one-week period with no noticeable effect. The success of Gilman, Kampf, and Sechi has been previously noted.

Sulfa drugs have been tried in a few cases. Turner and Zakon used sulfanilamide, 40 grains per day for 11 days, with no noticeable or subjective improvement. Sulfapyridine used subsequently gave similar results. On the other hand, Lewis³³ maintained a patient on one gram of sulfathiazole daily for the last month of her pregnancy with successful amelioration of all her subjective complaints. He advised further use of chemotherapy in the treatment of herpes gestationis, and admonished that once relief was obtained by the drug, prompt relapse of the disease would follow unless a maintenance dose were continued.

Fortunately, it is seldom necessary to induce premature labor in these cases, though it is the only method which will permanently allay symptoms in the majority of cases.

Gellhorn¹⁴ performed a cesarean section in a 34-year-old multipara who had gone three weeks past term, and showed no signs of impending labor despite four attempts at medical induction. Herpes gestationis had developed only two weeks before, and was rapidly becoming more severe. At operation, the patient was delivered of a normal 10½-pound infant. The mother died 4 days post partum of peritonitis and sepsis. The infection was thought to be due to the fact that the incision had to be made through diseased skin with its pus-filled vesicles which could not be sufficiently sterilized though particular precaution had been taken. No vaginal examination was performed at any time prior to operation. Carter and Pearse¹⁵ reported a similar case in which peritonitis developed 4 days postoperatively from a cesarean section for cephalopelvic disproportion, from which the patient successfully recovered.

Mayr,²⁵ in discussing the literature and reporting six cases of this disease, concluded that the only treatment for the severe cases of herpes gestationis is interruption of the pregnancy, and admonished that the physician should not hesitate to undertake this procedure.

Likewise, Adair and Stieglitz¹⁶ advise interruption of the pregnancy in all cases where therapeutic measures not contraindicated by the pregnancy have been tried and failed, and where the expectant woman's life or health are endangered, or the itching is so intense as to disturb the tranquillity necessary for an otherwise physiologic state to reach its normal end.

Two cases are herewith presented, with reference to the type of treatment and results obtained in each case.

Case Reports

CASE 1.—This patient was a 27-year-old white housewife, who was transferred to Kings County Hospital on November 25, 1942. Two weeks before, in another institution, she had been delivered at term of a 5 pound, 4 ounce living female infant. Shortly after delivery, she developed a generalized bullous and vesicular skin eruption which was severely pruritic. This had persisted despite treatment in the other institution, and was characterized by recurrent crops of vesicles and bullae.

Her pregnancy had been uneventful except for the appearance of urticarial-like macular and iris skin lesions on the hands and thighs in the fifth month of this pregnancy. These lesions had burned and itched severely. The patient noted several remissions and exacerbations of the rash; and only two weeks before delivery, she had a short-lived flare-up during which bullae and vesicles had appeared.

Past history was negative. This was her second pregnancy. The first had terminated spontaneously at 2½ months' gestation in November, 1941.

At the time of transfer to us, general physical examination was essentially negative except for the skin eruption. Few areas of clear skin remained. The bases of the various bullae consisted of erythematous halos. Some vesicles and bullae appeared to arise from normal skin. The larger bullae measured 1.5 centimeters in diameter at their bases. All of the bullae were under tension but did not rupture spontaneously. Some of the bullae had a purulent content. Several lesions were noted on the mucous membranes of the mouth.

Laboratory determinations were as follows: W.B.C. 12,000 with 81 polymorphonuclear leucocytes and 19 lymphocytes per 100 cells; hemoglobin determination 62 per cent. Blood Wassermann was negative. The blood urea was 22 mg. per 100 c.c. of blood; creatinine 1.17; and sugar 80. The sodium chloride determination was 485 mg. per 100 c.c. of blood. Urinalysis was negative.

A biopsy of one of the skin lesions was obtained. This was reported by the pathologists (Dr. W. W. Hala and Dr. Joseph Rini) as follows: "Section is one of skin in which continuity of the epidermal lining is disrupted by a ruptured bullous lesion, the cavity of which is filled with erythrocytes and serum. The epidermis shows hypertrophy with elongations and tree-like branching of the rete cones. Some intra- and intercellular edema is noted. There is moderate edema of the papillary bodies, with marked dilatation and congestion of the capillaries and

vascular channels, many of them containing perivascular infiltrations of eosinophiles and neutrophiles, some lymphocytes. Considerable endothelial proliferative activity is also present. Numerous eosinophiles and neutrophiles are present in the upper cutis."

The diagnosis clinically and pathologically was herpes gestationis.

Treatment was by abscission of the bullae, local applications, and daily permanganate baths. One blood transfusion was given for supportive measures. Sulfathiazole medication was tried on several occasions, but the patient always noted an increase in the intensity of the pruritus during the time of administration and the skin eruption likewise became more marked. The pruritus of the eruption could be alleviated temporarily by adrenalin hypodermically or by ephedrine sulfate orally.

The disease continued to be characterized by recurrent crops of vesicles and bullae, but each exacerbation was less severe than the previous one. On January 3, 1943, the patient was discharged from the hospital. At this time the skin was almost completely cleared up and the vital signs were normal. There have been no recurrences.

CASE 2.—The patient was a 19-year-old white Italian housewife who entered Kings County Hospital for the first time on November 19, 1940, because of a severe skin eruption associated with pregnancy. Eight days before admission, she had noted a small bleb below the umbilicus. During the next several days, a severely pruritic rash developed over the entire abdomen; and just before admission to the hospital, new lesions had developed on the arms, breasts, back, and thighs. Her last menstrual period had begun on April 21, 1940; and the expected date of confinement had been set as January 28, 1941. This was her first pregnancy. She had been receiving adequate prenatal care.

There was no previous history of skin diseases or allergic reactions. There had been no previous operations or serious illnesses except for influenza two years before.

Physical examination was essentially negative except for a generalized skin eruption, presenting erythematous urticarial-like lesions, varying in diameter from $\frac{1}{2}$ to $1\frac{1}{2}$ centimeters. Many of the lesions had small vesicular centers, confluent in several areas, notably over the entire abdomen, with small vesicles and bullae. Pelvic measurements were ample. The fundus of the uterus extended 3 fingers above the umbilicus. Fetal heart tones were good.

Laboratory data: R.B.C. 4,450,000 with 75 per cent hemoglobin. W.B.C. 28,450 with 56 per cent polymorphonuclear leucocytes, 16 per cent lymphocytes, and 28 per cent eosinophiles. Blood Wassermann was negative. Urinalysis was negative. Blood urea was 24 mg. per 100 c.c. of blood; creatinine 1.15; sugar 80.

A diagnosis of herpes gestationis was made clinically.

The course was characterized by severe remissions and exacerbations of the skin eruption. She complained of joint pains on several occasions. Treatment consisted of local applications of permanganate solution, abscission of the bullae, and by mouth both calcium gluconate and ephedrine sulfate.

On December 5, 1940, she went into labor spontaneously and after 10 hours, delivered without incident a premature 4 pound, 15 ounce male infant. The child was weak and lethargic, and lived only 24 hours.

Subsequent to delivery, there was no acute flare-up of the eruption. A few new crops of bullae and vesicles appeared from time to time, but the pruritus gradually became less. When discharged on December 30, 1940, her general condition was good and the skin lesions had almost completely disappeared, leaving areas of brownish pigmentation.

The patient was readmitted on July 17, 1942, at which time she was hospitalized for one week because of a spontaneous abortion of eight weeks' gestation. There were no skin lesions associated with this pregnancy. Postabortal course was uneventful.



Fig. 1.—Case 2. Seven days post partum. Note the large vesicles grouped together beneath the right breast.

The patient again entered Kings County Hospital on March 3, 1943. Six days before admission, the patient noted blebs over both feet associated with a severe pruritus. The lesions rapidly spread up the legs, and on admission had already appeared on the breasts and abdomen. She complained of a severe generalized burning and pruritus. Her last menstrual period had begun on November 15, 1942. Expected date of confinement had been placed on August 22, 1943.

Physical examination was again essentially negative except for the generalized skin eruption, consisting of erythematous plaques, bullae, and vesicles. Pelvic examination confirmed the diagnosis of an intra-uterine pregnancy of approximately 4 months' gestation.

A diagnosis of herpes gestationis was again made, and treatment was begun. Despite permanganate baths and topical applications of antiseptic lotions following abscission of the larger vesicles and bullae, the eruption and general condition of the patient became rapidly worse and a therapeutic abortion was considered. A remission then developed, and

conservative measures of treatment were continued with the hopes of maintaining the pregnancy until term.

Twice weekly for several weeks, injections intramuscularly of serum obtained from pregnant women of approximately the same gestational period were given. After each injection, the patient complained of a severely intense pruritus, and many new crops of lesions appeared. Autohemotherapy was likewise tried and similar results were obtained. Histamine, in the form of torantil tablets, units 20, were given twice daily for eight weeks with no essential relief. Sulfathiazole was resorted to on several of the exacerbations with no relief objectively or subjectively.

Supportive measures such as small repeated blood transfusions, liver extract intramuscularly, high vitamin and high caloric diet, etc., maintained the patient in fairly good general condition despite repeated exacerbations and remissions of the skin eruption. As the pregnancy progressed, the patient's mental status became more depressed and melancholic. At times, she complained of severe pruritus and burning. Occasionally, hot flashes were also noted objectively.

On May 16, the patient developed regular rhythmical uterine contractions which were very painful to her. The cervix seemed partially effaced on rectal examination, and the presenting part seemed to dip into the pelvis. Premature labor seemed impending, but several small repeated doses of morphine gave complete relief and the pregnancy continued normally thereafter. A similar episode was noted approximately one month later, on June 21.

Early in July, the patient developed an abscess in the right buttock following an intramuscular injection. An incision and drainage was performed, with the evacuation of 12 ounces of greenish purulent material. Culture of this revealed *Streptococcus hemolyticus* and *Staphylococcus aureus hemolyticus*. One week later, she developed a similar abscess in the suprascapular area which also had to be incised and drained. Both lesions healed rapidly following incision and drainage. Sulfanilamide was placed in both wounds.

The patient went into labor spontaneously on August 18, 1943. After a 9-hour labor, she was delivered spontaneously of a living 4 pound, 14 ounce healthy female infant.

Although the patient had had almost a complete remission of her skin eruption for two weeks prior to delivery, an acute exacerbation occurred almost immediately post partum. Numerous new skin lesions developed, and these were associated with an intense pruritus and burning. The patient was given massive doses of stilbestrol therapy without subjective or objective improvement. After two weeks, the eruption gradually subsided, the mental outlook improved, and only occasional new lesions appeared. She was discharged on September 18, 1943, at which time the general condition was good and the skin almost completely cleared.

The infant was discharged with the mother, and has remained in good health subsequently. It is interesting to note that the infant, though free of any lesions at delivery, developed a mild erythematous and maculopapular eruption on the face, chest and abdomen 6 hours later. This disappeared spontaneously on the third day of life.

Numerous laboratory tests were performed on the patient both before and after delivery. Urinalysis was negative throughout her course except for an occasional trace, or one-plus albuminuria. The white

blood cell counts varied between 9,000 and 18,000. There were a minimal number of eosinophiles noted on differential examination. The red blood cell count varied between 3.5 and 4.5 million cells per c.c. The sedimentation rate was 24 mm. in 45 minutes. Rh-factor was positive. (The father was also determined to be Rh-positive.) Prothrombin time was determined to be 80 per cent of normal. Blood urea ranged between 21 to 25 mg. per 100 c.c. of blood; sugar 76 to 78 mg. Prenatally, the albumin was found to be 3.5 with the globulin 2.9, a total protein value of 6.4. Cholesterol esters were 118, with free cholesterol 72. Total cholesterol determination was 190. Calcium was 9.9; phosphorus 3.4; and phosphatase 1.9 units. The van den Bergh was direct negative. Icterus index was 4.0. An x-ray examination of the chest revealed no old or recent pulmonary or pleural pathology. An electrocardiogram was normal.

Post partum, at the height of an acute exacerbation of the disease, a cephalin flocculation test was done to determine liver function, and this was reported as normal. On the tenth post-partum day, a Friedman test was performed and this likewise was reported as negative.

On October 7, 1943, the patient developed a severe generalized burning sensation with the reappearance of many new vesicles and bullae. She presented herself for readmission on October 10. Shortly after admission to the hospital, she began to menstruate for the first time post partum. This period lasted three days. With the subsidence of her menstrual flow, the lesions also began to disappear. The patient was discharged on October 17, at which time almost all the lesions had again disappeared. Diagnosis on discharge was herpes menstrualis recidivans. Several succeeding periods were likewise accompanied by the appearance of an eruption associated with pruritus, but each time the course was less severe and soon subsided. Her general condition is good at present.

Summary

1. Two cases of herpes gestationis with reference to their treatment and results obtained therefrom, have been presented. The previous literature has been reviewed.

2. Herpes gestationis is a polymorphous exanthema differentiated from similar forms because of its etiology rather than its morphologic characteristics.

3. The disease is characterized by its chronicity, with remissions and exacerbations throughout the course of gestation; and by a tendency to recur in subsequent pregnancies with increasing severity.

4. The disease responds poorly, if at all, to any form of therapy.

5. The prognosis for the mother is good; it is less so for the offspring. Many cases can be carried to full term in spite of the disease.

The authors are indebted to Doctor E. A. Gauvain and Staff of the dermatological service at Kings County Hospital for the privilege of presenting the dermatological aspects of these cases.

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2104 FOSTER AVENUE
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ORAL SUBSTITUTION THERAPY WITH ETHINYL ESTRADIOL AND ALPHA-ESTRADIOL

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WITHIN recent years a new phase in ovarian substitution therapy—the oral phase—has been developed. With injection therapy previously favored by the availability of potent hypodermic preparations, a return to the oral method of treatment has been initiated by the discovery and manufacture of active, orally effective estrogenic substances such as diethylstilbestrol, ethinyl estradiol and conjugated estrogens equine.

The Endocrine Department of this clinic was founded in 1930, and since that time several thousand women have been treated with estrogens for ovarian deficiency. Following this background of unpublished material, data have been kept and published on 502 patients treated orally and hypodermically with estrone, estradiol benzoate and diethylstilbestrol dipropionate.¹ An additional report has been made on 138 patients treated orally with conjugated estrogens equine.² In the present study, the clinical response of 47 patients to ethinyl estradiol has been tabulated along with previously unpublished observations on 80 patients treated with oral alpha-estradiol (dihydroxyestrin). It has thus been possible to compare the relative clinical effectiveness of six estrogenic substances which have been employed in the treatment of 767 patients.

Ethinyl Estradiol

Reports appearing in the literature on ethinyl estradiol appear to be quite favorable.^{8, 9, 12-16} This estrogen was prepared in 1938 by Inhoffen and Hohlweg^{17, 18} by replacement of the hydrogen of the seventeenth carbon atom in estradiol with an ethinyl group. In our studies, enteric coated ethinyl estradiol tablets* of 0.01 mg., 0.02 mg., 0.05 mg., and 0.1 mg. were used. Uncoated tablets of 0.05 mg. were also employed.

A total of 47 patients ranging in age from 24 to 60 years were treated with ethinyl estradiol. Included in this series were 17 cases of natural menopause, 15 cases of artificial menopause and 15 other cases, part of which were associated with hypoestrinism. Results in this series are summarized in Table I.

Analysis of Results With Ethinyl Estradiol

When ethinyl estradiol was given, it was possible to duplicate any therapeutic effect obtained with diethylstilbestrol dipropionate. Furthermore, equally effective results were obtained with smaller amounts of material. Indeed, it was observed that a dose as low as 0.02 mg. of ethinyl estradiol produced a definite therapeutic response. While

*The ethinyl estradiol tablets (Estinyl) used in this investigation were supplied through the courtesy of Dr. Max Gilbert and Dr. William R. Bond of the Schering Corporation, Bloomfield, N. J.

TABLE I. RESULTS WITH ETHINYL ESTRADIOL*

| PATIENT | AGE | REMARKS (A) | HOT FLASHES | NERVOUSNESS | MENSTRUATION (B) | SPECIAL TYPE (C) | DAILY DOSE IN MG. | REACTIONS (D) | UTERINE BLEEDING (E) | VAGINAL SMEARS (F) | | % RELIEF OBTAINED |
|----------------------|-----|-------------------------------------|-------------|-------------|------------------|------------------|-------------------|---------------|----------------------|--------------------|-------|-------------------|
| | | | | | | | | | | BEFORE | AFTER | |
| NATURAL MENOPAUSE | | | | | | | | | | | | |
| 1. Mrs. K. B. | 51 | | ++ | ++ | O | | 0.05 | 0 | | 4 | | 100 |
| 2. Mrs. N. K. | 47 | M | +++ | ++++ | O | | 0.1 | 0 | B | 2 | 1 | 100 |
| 3. Mrs. L. L. | 48 | M; IN; P; A | +++ | +++ | O | | 0.05 | 0 | | 4 | 4 | 100 |
| 4. Mrs. E. T. | 50 | H; IN; M | ++++ | +++ | O | | 0.1 | 0 | | | | 50 |
| 5. Mrs. M. R. | 51 | Worried | ++++ | ++++ | O | | 0.2 | 0 | | | | 100 |
| 6. Miss F. M. | 42 | A; P | ++++ | ++++ | O | | 0.06 | 0 | | | | 75 |
| 7. Mrs. A. T. | 46 | | ++++ | +++ | O | | 0.1 | 0 | B | 2 | 1 | 50 |
| 8. Miss M. W. | 41 | IN | ++ | +++ | I | | 0.05 | 0 | | | | 100 |
| 9. Mrs. M. W. | 56 | IN | ++++ | ++ | O | | 0.1 | 0 | | | | 100 |
| 10. Mrs. E. R. | 49 | H | ++++ | + | O | | 0.05 | 0 | | | | ? |
| 11. Miss L. B. | 45 | A; M | +++ | ++ | R | | 0.1 | 0 | | | | 50 |
| | | | | | | | 0.2 | 0 | | | | 100 |
| | | | | | | | 0.01 | 0 | | | | 0 |
| | | | | | | | 0.02 | 0 | | | | 25 |
| | | | | | | | 0.05 | 0 | | | | 50 |
| 12. Mrs. F. B. | 51 | | ++++ | +++ | O | | 0.1 | 0 | B | 1 | | 100 |
| | | | | | | | 0.05 | 0 | | | | 50 |
| | | | | | | | 0.1 | 0 | | | | 85 |
| 13. Mrs. B. O. | 48 | A; H | ++ | + | I | | 0.2 | 0 | | 1 | | 100 |
| | | | | | | | 0.02 | 0 | | | | 50 |
| | | | | | | | 0.05 | 0 | | | | 100 |
| 14. Mrs. R. L. | 40 | Menstruates only part of one day; M | ++ | +++ | | | 0.1 | 0 | | 3 | 3 | 100 |
| | | | | | | | 0.01 | 0 | | | | 0 |
| | | | | | | | 0.02 | 0 | | | | 10 |
| | | | | | | | 0.05 | 0 | | | | 50 |
| 15. Mrs. A. R. | 56 | | + | + | O | | 0.1 | 0 | | 2 | | 100* |
| 16. Mrs. I. D. | 50 | | + | + | O | | 0.01 | 0 | | | | 50 |
| | | | | | | | 0.02 | ? | | | | 100 |
| 17. Mrs. N. D. | 60 | IN; M | ++++ | +++ | O | | 0.05 | 0 | | | | 75 |
| ARTIFICIAL MENOPAUSE | | | | | | | | | | | | |
| 18. Miss E. M. | 56 | A; M; H | ++ | ++ | O | U | 0.01 | 0 | | 1 | | 0 |
| | | | | | | | 0.02 | 0 | | | | 25 |
| | | | | | | | 0.05 | 0 | | | | 50 |
| | | | | | | | 0.1 | 0 | | | | 100 |
| 19. Mrs. C. O. | 33 | A; P; H | ++++ | ++++ | O | 2—O | 0.1 | 0 | | 4 | 3 | 100* |
| 20. Mrs. O. P. | 52 | A | ++++ | +++ | I | X | 0.02 | 0 | | | | 25 |
| | | | | | | | 0.05 | 0 | | | | 75 |
| | | | | | | | 0.1 | 0 | | | | 100 |
| 21. Mrs. P. A. | 42 | A | ++++ | ++++ | O | U | 0.1 | ? | | 1 | | 50 |
| | | | | | | 1½—O | 0.3 | 0 | | | | 85 |
| 22. Miss A. M. | 52 | A | ++++ | ++ | O | U | 0.1 | 0 | | | | 50 |
| | | | | | | 2—O | 0.2 | N, D | | | | 85 |
| 23. Mrs. R. B. | 44 | A; H | + | ++ | O | U | 0.1 | 0 | | 2 | | 50 |
| | | | | | | 2—O | 0.2 | 0 | | | | 65 |
| 24. Mrs. S. C. | 53 | A; G | ++ | +++ | O | X | 0.1 | 0 | B | | | 85 |
| 25. Mrs. R. S. | 38 | F; M | + | ++++ | O | U | 0.1 | ? | | 2 | | 50* |
| | | | | | | 1—O | | | | | | |
| 26. Mrs. S. S. | 45 | | ++++ | +++ | O | 2—O | 0.05 | 0 | | | | 100 |
| | | | | | | | 0.1 | 0 | | | | 100 |

*See Key to Table I, page 184.

TABLE I—CONT'D

| PATIENT | AGE | REMARKS (A) | HOT FLASHES | NERVOUSNESS | MENSTRUATION (B) | SPECIAL TYPE (C) | DAILY DOSE IN MG. | REACTIONS (D) | UTERINE BLEEDING (E) | VAGINAL SMEARS (F) | | % RELIEF OBTAINED |
|----------------------|-----|--|-------------|-------------|------------------|------------------------------|------------------------------|------------------|----------------------|--------------------|-------|----------------------|
| | | | | | | | | | | BEFORE | AFTER | |
| ARTIFICIAL MENOPAUSE | | | | | | | | | | | | |
| 27. Mrs. F. M. | 47 | H; husky voice; emotional | ++++ | +++ | O | 2—O | 0.01 0.02 0.04 0.05 | 0 0 0 0 | B | 3 | 1 | 0 35 75 100 |
| 28. Mrs. G. W. | 38 | C; M; H | + | ++++ | O | 1 $\frac{1}{2}$ —O X U | 0.1 0.01 0.2 | V 0 N | | | | 100 100 20 |
| 29. Mrs. J. M. | 35 | A; H | ++ | ++ | O | 1 $\frac{1}{2}$ —O U | 0.05 0.05 | N 0 | | 4 | | 100* 75 50 |
| 30. Mrs. H. M. | 46 | A | +++ | ++ | O | 1—O 2—O U | 0.1 0.1 | 0 N | | | | 100 100 |
| 31. Mrs. C. M. | 38 | M | ++++ | + | O | 2—O U | 0.1 | N | | 2 | 1 | 100 |
| 32. Mrs. H. W. | 31 | A; IN; M | ++++ | +++ | O | 2—O U | 0.05 0.1 | 0 0 | | | | 50 90 |
| OTHER CASES | | | | | | | | | | | | |
| 33. Miss F. C. | 44 | A; H; treatment given for therapeutic test | 0 | +++ | O | U | 0.1 | 0 | | 1 | | 0 |
| 34. Mrs. M. R. | 36 | A; H; SA; (G) | 0 | + | O | | 0.1 | 0 | | 2 | | 35 |
| 35. Mrs. A. M. | 29 | M; S; marital trouble | + | ++++ | R | 1—O | 0.05 0.1 | 0 0 | L | 1 | | 25 35* |
| 36. Mrs. E. O. | 31 | A; F | 0 | ++ | R | | 0.1 | 0 | L | 2 | | 50* |
| 37. Mrs. E. W. | 29 | A; H; P; SA | + | ++++ | I | | 0.05 0.1 | 0 0 | | | | 0 25* |
| 38. Miss H. A. | 24 | SA | 0 | 0 | O | | 0.1 | N V | | | | |
| 39. Mrs. A. H. | 25 | A; DM; F; trochanteric obesity | 0 | ++ | I | | 0.05 0.1 | 0 0 | | | | 50 50* |
| 40. Miss I. R. | 36 | | + | ++ | R | | 0.1 | 0 | L | 4 | 1 | 100 |
| 41. Mrs. P. S. | 36 | Eunuchoid; infantile uterus; menstruation began age 17; F; S | + | + | R | | 0.05 | T | B | 2 | | 100* |
| 42. Mrs. M. S. | 37 | Manic depressive psychosis; treatment given for therapeutic test | 0 | ++++ | I | 1 $\frac{1}{2}$ —O | 0.1 | 0 | | 2 | | 0 |
| 43. Mrs. F. D. | 37 | A; F; M; C | 0 | ++++ | R | | 0.05 | 0 | L | 2 | 1 | 50* |
| 44. Mrs. M. M. | 53 | Psychoneurosis; treatment given for therapeutic test | ? | ++++ | O | | 0.01 0.02 0.1 | 0 0 ? | | 3 | | 0 0 0* |
| 45. Mrs. M. K. | 29 | Hypopituitary; secondary hypovarian; ht. 57 in.; primary amenorrhea and asthenia | 0 | + | O | | 0.05 | N T | | | | 0 |
| 46. Mrs. M. P. | 34 | Headaches at menstruation | 0 | + | R | | 0.1 | 0 | | 4 | 3* | 50 |
| 47. Mrs. J. R. | 47 | A; C; M | 0 | +++ | R | | 0.03 0.1 | 0 ? | | 2 | | 25 0 |

some patients required as much as 0.2 mg., optimal dosage for most patients averaged 0.05 mg. to 0.1 mg. The average per cent of improvement on ethinyl estradiol at various dosage levels is tabulated below:

| DOSE IN MG. | | 0.01 | 0.02 | 0.05 | 0.1 | 0.2 |
|----------------------|-------------|------|------|------|-----|-----|
| Natural menopause | Improvement | 17% | 46% | 64% | 86% | 95% |
| Artificial menopause | Improvement | 7% | 28% | 71% | 83% | 83% |
| Other hypo-ovarian | Improvement | | | 37% | 31% | |

Mental depression in the menopause proved most refractory to therapy. However, ethinyl estradiol was much more beneficial than any of the other natural estrogens used. In this respect, its action was similar to that afforded by diethylstilbestrol dipropionate.

Vaginal smears were normal in 6 of 27 patients examined before treatment, while the remaining 21 patients showed varying degrees of estrogen deficiency. Ten of these patients had vaginal smears taken after treatment and improvement was noted in eight cases. Excessive discharge and infections of the vagina and cervix frequently prevented the use of this test for assay.

Undesirable Effects With Ethinyl Estradiol

Menstrual bleeding was caused by ethinyl estradiol in five patients who were no longer menstruating because of artificial or natural menopause. Menstruation was delayed in four patients who always menstruated regularly and it was very profuse in another patient.

True toxic reactions to ethinyl estradiol were observed in seven patients with the following symptoms: nausea—five; vomiting—two; dizziness—one; nervousness—one; and “generally worse and more tense”—one. Patient 22 had nausea and dizziness on 0.2 mg. but not with 0.1 mg. Patient 28 had vomiting on 0.1 mg. but not on 0.01 mg. Patient 29 had nausea on 0.2 mg. but on 0.05 mg. this became markedly

KEY TO TABLE I

- (a) A—Asthenia; C—Difficulty thinking and concentrating; DM—Dysmenorrhea; F—Frigidity; G—Globus; H—Headache; IN—Insomnia; M—Mental depression; P—Palpitation; S—Sterility; SA—Secondary amenorrhea.
 (b) I—Irrregular; 0—No longer menstruating; R—Regular.
 (c) O—Ovaries removed; U—Uterus removed; X—X-ray menopause.
 (d) D—Dizziness; N—Nausea; T—“Nervous tension;” V—Vomiting.
 (e) B—Some type of uterine bleeding or menstruation caused by the tablets; L—Tablets caused menstruation to be late.
 (f) 1—Normal; 2—Slight deficiency of estrogen; 3—Moderate deficiency; 4—Severe deficiency.
 (g) Pituitary tumor; Hirsutism; Hormone assay of urine: 19 C.U. of androgens per 24 hours.

*Remarks after treatment: Patient 15 had a constant pain at the end of the urethra which was not relieved; Patient 19 had had a nervous breakdown from which she did not recover; Patient 25 had improvement in hot flashes and breast soreness only; Patient 29 had migraine headaches from which she obtained no relief; Patient 35 had a marked increase in the size of her breasts; Patient 36 had an increase in her libido associated with a lessening in asthenia and nervousness; Patient 37 had an increase in libido and in the size of her breasts; Patient 39 had less asthenia and nervousness, but she was not otherwise benefited; Patient 41 had relief of the hot flashes, but the menstruation, which was scanty before treatment, became more profuse and painful; Patient 43 had fifty per cent improvement of symptoms, but the effect was at least partly pharmacodynamic; Patient 44 had an increase in the “sweats” on 0.1 mg., proving that they were not hot flashes. Breast soreness developed showing effectiveness of material; Patient 46 had abnormal vaginal smears because of marked vaginitis.

reduced. While no attempt was made to use smaller dosage with the other cases, it was evident that the above three patients improved when the dose was decreased and it is believed that most patients would tolerate small amounts of the drug.

Toxicity for the entire group, covering all dosage levels, was 14 per cent, but the incidence was very much less with doses under 0.05 mg. daily.

There were five questionable reactions on ethinyl estradiol. With patient 16 insomnia developed while 0.02 mg. was being taken but later disappeared although the tablets were continued. Dizziness began in patient 21 with 0.1 mg. but cleared up when 0.3 mg. was taken. Patient 25 developed a "gnawing in the stomach" on 0.1 mg. but this symptom was noticed occasionally before taking the tablets. Patient 44 began to "sweat" more with 0.1 mg. but not with smaller doses. Patient 47 had a poor appetite on 0.1 mg. but tolerated 0.03 mg.

There was an increase in fullness and tenderness in the breasts in many cases treated with ethinyl estradiol, and three patients complained of severe soreness. Several mentioned that the nipples and areola darkened in color; while others, in whom breast soreness was present before treatment reported improvement while taking the tablets. Several patients noted an increase in vaginal moisture or leucorrhea during treatment. This has also been observed when other potent estrogens are employed, either orally or parenterally.

Eleven of the patients who had no reactions with enteric coated tablets of ethinyl estradiol were given 0.05 mg. uncoated tablets. None of these patients had a reaction, and symptoms were relieved as effectively with the uncoated tablets as with the enteric coated tablets.

Alpha-Estradiol

The uncoated tablets of alpha-estradiol* (dihydroxyestrin) a natural estrogenic substance found in the ovary and blood of human beings, were standardized by weight to contain 0.1 mg., 0.2 mg. and 0.5 mg. They were taken from one to three times daily depending on the dose prescribed. Alpha-estradiol was also obtained as a stable, chemically pure, crystalline substance. It was highly insoluble in water, but some of it was dissolved in sesame seed oil with the use of a solvent. This oil, containing various amounts of alpha-estradiol, was taken by patients in 20 drop doses, three times daily.

The following doses represent the largest amount of alpha-estradiol given to each patient per day.

| DAILY DOSE OF ALPHA-ESTRADIOL | NUMBER OF PATIENTS | DAILY DOSE OF ALPHA-ESTRADIOL | NUMBER OF PATIENTS |
|----------------------------------|-----------------------|----------------------------------|-----------------------|
| 0.2 mg. | 5 | 0.8 mg. | 2 |
| 0.3 mg. | 2 | 1.0 mg. | 10 |
| 0.4 mg. | 17 | 1.5 mg. | 9 |
| 0.5 mg. | 27 | 2.0 mg. | 1 |
| 0.6 mg. | 6 | 3.0 mg. | 1 |

Results With Alpha-Estradiol

While a favorable response was obtained with alpha-estradiol administered orally as tablets, improvement was definitely less in degree. Only patients with milder symptoms who did not wish to take injections were given alpha-estradiol. Sedatives were not used in any of the cases.

*These tablets, called Progynon-DH, were obtained from the Schering Corporation, Bloomfield, N. J.

Alpha-estradiol, orally, did not relieve hot flashes very well in doses less than 0.5 mg. daily, and a better response was obtained with 1.5 mg. daily. This natural estrogen had a good tonic effect and increased the sense of well-being in patients.

Results regarding migraine, dysmenorrhea, premenstrual tension, etc., are not included since these conditions were frequently not associated with hypoestrinism, and improvement in each case was predicated on the response to estrogens of patients with hypoestrinism. However, where these conditions were associated with the syndrome, they were frequently relieved by estrogen therapy. In some instances it was felt that the pharmacodynamic or drug action of the estrogen was responsible for relief. This has been noted frequently in previous observations with diethylstilbestrol dipropionate.

Toxicity With Alpha-Estradiol (Oral)

In general, untoward reactions to alpha-estradiol were negligible. While taking alpha-estradiol, 1 mg. daily, one patient began to flow early, one late and one had severe dysmenorrhea. Only one patient developed nausea and vomiting, a reaction caused by many other types of medication. There was no true toxicity. One patient felt nervous and more tense. Hyperestrinemia might have existed previously in this patient since the breasts had been sore and firm for two years. Unfortunately, a hormone assay of the urine was not made in this case. Two other patients receiving alpha-estradiol complained of breast soreness. Hormone assays of some of the other patients treated in this series have been reported previously.⁴

Comparison With Other Oral Estrogens

After this study, it is possible to evaluate the strength of six estrogenic substances used at the clinic. The data on estrone, estradiol benzoate, diethylstilbestrol dipropionate¹ and conjugated estrogens-equine² were obtained from previous observations. Their relative strengths, judged on a weight basis milligram per milligram, are listed in Table II. Other desirable and undesirable results are also estimated as to degree of importance.

It was impossible to obtain a strong estrogenic effect with estrone, estradiol benzoate or alpha-estradiol with the amount of material given, such as was produced by conjugated estrogens, diethylstilbestrol dipropionate or ethinyl estradiol. Of course, the hypodermic administration of estrone and estradiol benzoate gave a strong estrogenic response, the latter being stronger than the former, but the comparison in Table II was limited to material absorbed from the gastrointestinal tract. One milligram of conjugated estrogens-equine was roughly equivalent to 0.3 mg. to 0.5 mg. of diethylstilbestrol dipropionate or 0.05 mg. to 0.1 mg. of ethinyl estradiol. Since the strong effect of 0.05 mg. to 0.1 mg. of ethinyl estradiol was not produced by alpha-estradiol⁶⁻¹¹ in the doses used, 1 mg. to 1.5 mg., it was known that ethinyl estradiol was at least 15 to 30 times more effective than alpha-estradiol. While Hohlweg and Inhoffen¹⁷ reported that ethinyl estradiol was 15 to 20 times as effective as alpha-estradiol. Soule^{6, 9} stated that it was 50 to 70 times as effective. Thus, in adding the ethinyl radical to alpha-estradiol, a potent estrogen effect has been obtained with greater economy.

TABLE II. EFFECT OF ESTROGENS GIVEN

| 1 MG. OF EACH | ESTRONE | ESTRADI- OL BEN- ZOATE | ALPHA- ESTRA- DIOL | CONJU- GATED ESTRO- GENS | DIETHYL- STILBESTROL DIPROPION- ATE | ETHINYL ESTRADIOL |
|--|----------------|------------------------------|--------------------------|-----------------------------------|--|----------------------|
| Quantitative | Very little | Some | More | Strong | Stronger | Strongest |
| Qualitative | Good | Good | Good | Good | Not as good | Good |
| Uterine bleeding | 0 | ? | ? | + | ++ | +++ |
| Development of breasts | 0 | Slight | Slight | Good | Stronger | Strongest |
| Relief of mental depression | 0 | ? | + | +++ | ++++ | +++++ |
| Relief of hot flashes | Very little | Some | More | Strong | Stronger | Strongest |
| Toxicity per opti- mum effective dose | 0 | 0 | 0 | 0 | + | + |

Discussion

The oral method has several obvious advantages over the hypodermic. It is cheaper, timesaving and more convenient to the patients and doctor. It avoids local reactions frequently obtained with hypodermic injections.⁵ It allows frequent administration of material which has proved to be advantageous, as pellet implantation of hormone³ is more effective than intermittent doses by injection.

The oral method also has some disadvantages. Patients are inclined to treat themselves, while the hypodermic method permits constant management by the physician. The stronger preparations have a toxic effect on some patients. This toxicity is of a very mild nature and diminishes when the dosage is cut. In some patients a small dose was well tolerated whereas a larger amount caused symptoms of toxicity. Gastrointestinal symptoms are believed to be central, possibly medullary, rather than local in origin. Enteric coating of the tablets did not prevent the symptoms. Patients who tolerated enteric coated tablets also tolerated noncoated tablets. Prior to this study, patients who had had a toxic reaction to diethylstilbestrol dipropionate administered orally were given injections, but the nausea and vomiting still persisted. The toxic manifestations cleared up rapidly when medication was discontinued, leaving no permanent effect that was discernible. The symptoms were similar to those of early pregnancy, and although the patients generally asked to be permitted to stop taking the tablets, they did not feel that they had been harmed by the medicine.

With ethinyl estradiol, seven of the patients in this study (14 per cent) had a true toxic reaction. During the treatment of 109 patients reported in five papers,^{9, 12-14, 16} there were 13 reactions (11 per cent toxicity). Kurzrok, Birnberg and Livingston¹⁵ gave ethinyl estradiol to 59 patients after delivery to prevent lactation. In their series there was no evidence of toxicity. Of course, it is a well-known fact that patients who have recently been pregnant tolerate large doses of estrogenic substances.

It was interesting to note that the optimum daily dose of ethinyl estradiol in this series was low (0.05 mg. to 0.1 mg.). According to the literature, most of the treatment was with doses of 0.3 mg. to 0.45 mg. The puerperal cases were given up to 2.4 mg. However, in two of the papers, the effective dose was considered to range from 0.05 mg. to 0.15 mg.

The three estrogens that produced a greater response in the patient were believed to be less affected by the liver. The other estrogens going through the portal circulation did not reach the general circulation in sufficient concentration to be very beneficial. However, sublingual administration was shown to be very much more effective.¹⁹ It is believed that this method of administration, like the hypodermic injection, puts the hormone into the general circulation without its first having to pass through the liver, where it is partly inactivated.

Summary

Ethinyl estradiol was the most potent oral estrogen used up to the present time. Satisfactory relief of hypo-ovarian symptoms was usually obtained with 0.05 mg. to 0.1 mg. daily although larger doses were occasionally necessary. Its effect was compared to that of alpha-estradiol and to estrone, estradiol benzoate, diethylstilbestrol dipropionate and conjugated estrogens-equine previously studied. Of this group, ethinyl estradiol and diethylstilbestrol dipropionate caused mild toxic reactions in an occasional patient without apparent permanent harm. Keeping the dose down to the minimum needed for maximum effectiveness reduced the toxic symptoms. The addition of the ethinyl radical greatly increased the effectiveness of alpha-estradiol, thus reducing the cost of treatment. The oral method of treatment had many advantages.

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HYSTEROSALPINGOGRAPHY, A ROUTINE AID IN GYNECOLOGICAL DIAGNOSIS

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VISUALIZATION of the female genitalia in a group of fifty-two selected patients has proved a practical and innocuous procedure by which a more accurate knowledge of numerous pelvic conditions was obtained. The simplicity and clinical safety of hysterosalpingography with the use of the recently introduced opaque medium, Viscorayopake, warrant its adoption, routinely, for both office and hospital use.

Many pathologic growths of the female generative tract were clearly defined by this method and, in many cases, unsuspected lesions were revealed. The alteration in size and contour of the uterine shadow indicates not only the extent and location of new growths, but also identifies the type of tumor by means of characteristic and representative patterns. Since the length, course and patency of the Fallopian tube, as well as the presence of new growths, can be determined by x-ray, problems of sterility lend themselves particularly to its use. When employed with tubal insufflation as described by Rubin^{1, 2} complete knowledge as to both structure and function of the tube is obtained. In certain instances, tenuous peritubal adhesions causing obstruction to ovular migration, may undergo lysis following passage of the viscous radiopaque fluid. Salpingography served not only to differentiate between intrapelvic masses, but also between abdominal tumors from those of pelvic origin. In my experience, this test has often been a guide to correct operative procedure and surgical conservatism.

The stereoptical roentgen technique in hystero-radiography was also utilized to advantage. By this method, the relative intrapelvic position and size of anatomic structures and growths were determined, rendering an expressive picture in all dimensions.

Since 1910, when Rindfleisch³ first introduced hystero-radiography, many media have been used by various investigators. Leloirier,⁴ W. H. Carey,⁵ I. C. Rubin,⁶ W. T. Kennedy,⁷ J. A. Sicard,⁸ T. Neustaedter,⁹ and P. Titus¹⁰ have contributed largely to the development of hysterosalpingography in the past three decades. The radiopaque substances^{11, 12} such as Collargol,¹³ halogen salts, Lipiodol,¹⁴ Iodopine, iodized oils⁶ and the crystalline iodine compounds, Uroselectan,¹⁵ Diodrast¹⁶ and Hipuran,¹⁷ proved disadvantageous for clinical usage. These were eventually discarded because of various shortcomings, such as (1) unsatis-

*The opinions and assertions contained in this paper are the personal ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

factory opacity, (2) tissue irritation, (3) foreign body reaction due to retarded absorption, (4) insufficient viscosity, (5) toxicity and (6) chemical instability.

In the present studies, the fluid substance, viscorayopake,* was used. First introduced for clinical trial by I. C. Rubin¹⁶ at the Mt. Sinai Hospital, New York City, in 1941, it has fulfilled the requisites for an adequate and satisfactory opaque medium for pelvic x-ray. Nontoxic, quickly absorbed, chemically stable and amply viscous, it is easily administered, and does not gel or crystallize at room temperatures.

Method

This test may be employed in any properly equipped office or hospital. The technique is uncomplicated and safe. The patient is given two drams of licorice powder the night before and an enema on the morning of the test. The patient is placed on a Squier genitourinary x-ray table in lithotomy position, and a bimanual examination is performed to determine the cervico-uterine angle (for direction of canal) and the fundal size (for estimation of its capacity).

Aseptic technique is observed. The vulva and vagina are thoroughly cleansed with soap and water and the patient is draped with sterile towels.

The cervix, visualized through a nonopaque, bivalved speculum, is wiped dry and the external os is painted with tincture of iodine. A tenaculum forceps may be applied, but I found no advantage in this painful procedure, except in cases requiring traction for better cervical exposure, or, for a stenotic cervix resisting insertion of the cannula, or, where pressure against the cannula guard was necessary to prevent leakage.

A 20 c.c. syringe, containing 15 c.c. of viscorayopake,¹⁹ is fitted by means of a Luer metal tip to a uterine stem cannula with perforated end (as used in the Rubin insufflation test), or, when desirable, to a Colvin²⁰ cervical stainless steel screw-tip cannula. The latter eliminates the danger of uterine perforation and, in some cases, has been found satisfactory in preventing backflow. Upward pressure of the syringe piston displaces air from the syringe and its contained opaque fluid. If the medium injected into the uterine cavity contains air bubbles, errors in diagnosis are prone to occur. The cannula is then cautiously inserted through the external os, following the line of the cervico-uterine axis, until the perforated tip lies within the cavity. If the Colvin device is used, the screw-tip is rotated until it becomes firmly fixed in the cervical canal.

Excessive traction, or upward pressure on the cervix may cause uterine displacement producing shadow overlapping of the cavity outline. It is therefore advisable, before x-rays are taken, to replace the fundus so that it lies in a plane somewhat parallel to the x-ray plate.

With the cannula held in the cervix, the patient is moved into proper position under guidance of the x-ray technician, so that the x-ray tube and plate are in proper alignment with the pelvis.

I have used, ordinarily, for a 20-centimeter body thickness, 50 milliamperes and 58 primary volts for a two-second exposure with the focal plate distance between thirty and thirty-six inches.

*Chemical structure: Diethanolamine salt of 2, 4,-dioxo-2-iodo-6 methyl tetrahydropyridine acetic acid. Three and one-half per cent concentration of polyvinyl alcohol is added to procure satisfactory viscosity.



Fig. 1.—Hysterosalpingogram showing unilateral tubal patency and small uterus. Note left pelvic lipodol shadows appearing also in the original flat plate, or secret film.



Fig. 2.—X-ray film of a submucous fibroid delineated by viscorayopake and carbon-dioxide contrast media.

A flat plate or scout film is first taken. This often reveals calcified lymph nodes, phleboliths, or unabsorbed lipiodol used in previous tests, and is of value in excluding misleading shadows (Fig. 1). Two c.c. of radiopaque fluid are then injected very slowly, and a second plate is taken. By delivering the viscous medium into the uterine cavity very gradually, with light or moderate pressure, the patient is spared unnecessary pain. Two c.c. injections are repeated until 6 or 8 c.c. of viscorayopake and four or five x-ray films have been used. At this point, the fluid contents of the uterine cavity may be removed by withdrawing the piston.

The syringe is disconnected from the cannula, and about 10 to 15 c.c. of CO₂ gas, from a second clean syringe, are then injected into the uterine cavity. Another plate is taken while piston pressure is maintained. Hysteroaerography¹⁷ delineates cavity and tumor outlines by contrast of the gas with the viscorayopake film adherent to the uterine wall (Fig. 2). Contrast media provide additional means for obtaining more accurate x-ray plates.

Two c.c. of fluid are the optimum quantity used for any single injection; this amount is sufficient to render progressive silhouette changes required for comparative serial-film studies. Enlarged uterine cavities or tubal dilatations sometimes require up to 15 c.c. of opaque medium. In one instance of uterine cavity enlargement due to fibroids, 24 c.c. were injected without deleterious effect. (Fig. 3.)

A forty-five minute follow-up x-ray picture will very often show the excretion of the opaque fluid in the renal tract as well as its partial or complete absence from the pelvis (Fig. 4). Absorption and excretion of viscorayopake are rapid.

With each injection, the patient was asked to point with a finger to areas of discomfort or pain, and as the medium traversed the uterine cavity and the patent tubes, the finger moved laterally from the suprapubic midline. Patency, as well as the location of tract obstruction, was often clinically predetermined in this way.

The patient sits up within fifteen minutes after the last injection, and, in most instances, is immediately ambulatory. Transitory nausea and vomiting were observed infrequently among the entire group of fifty-two patients. Thirty-two women, or sixty-one per cent, were entirely free of discomfort or pain during or after the injections. Fifteen, or twenty-nine per cent, complained on questioning, of either discomfort, or mild but bearable pain, and five, or ten per cent, manifested severe and painful reactions, lasting from forty-five minutes to twenty-six hours. Two of these patients were relieved by codeine sulfate, while sedation, bed rest and a heating pad were sufficient to control the symptoms in the remaining three instances. In eight patients, or fifteen per cent, the application of the tenaculum, or traction on the cervix caused pain.

In two patients with a history of childhood convulsions and syncope, a definite *petit mal* syndrome occurred following the second injection. In both instances, however, recovery was immediate and there were no sequelae.

Where marked nervousness or apprehension is present, mild sedation should be used in preparation for the test.

Acute pelvic diseases, gonorrhea, intrauterine or ectopic pregnancy, cervical carcinoma or infection, and epilepsy contraindicate the use of hysterosalpingography. It is wise to postpone the test until after the

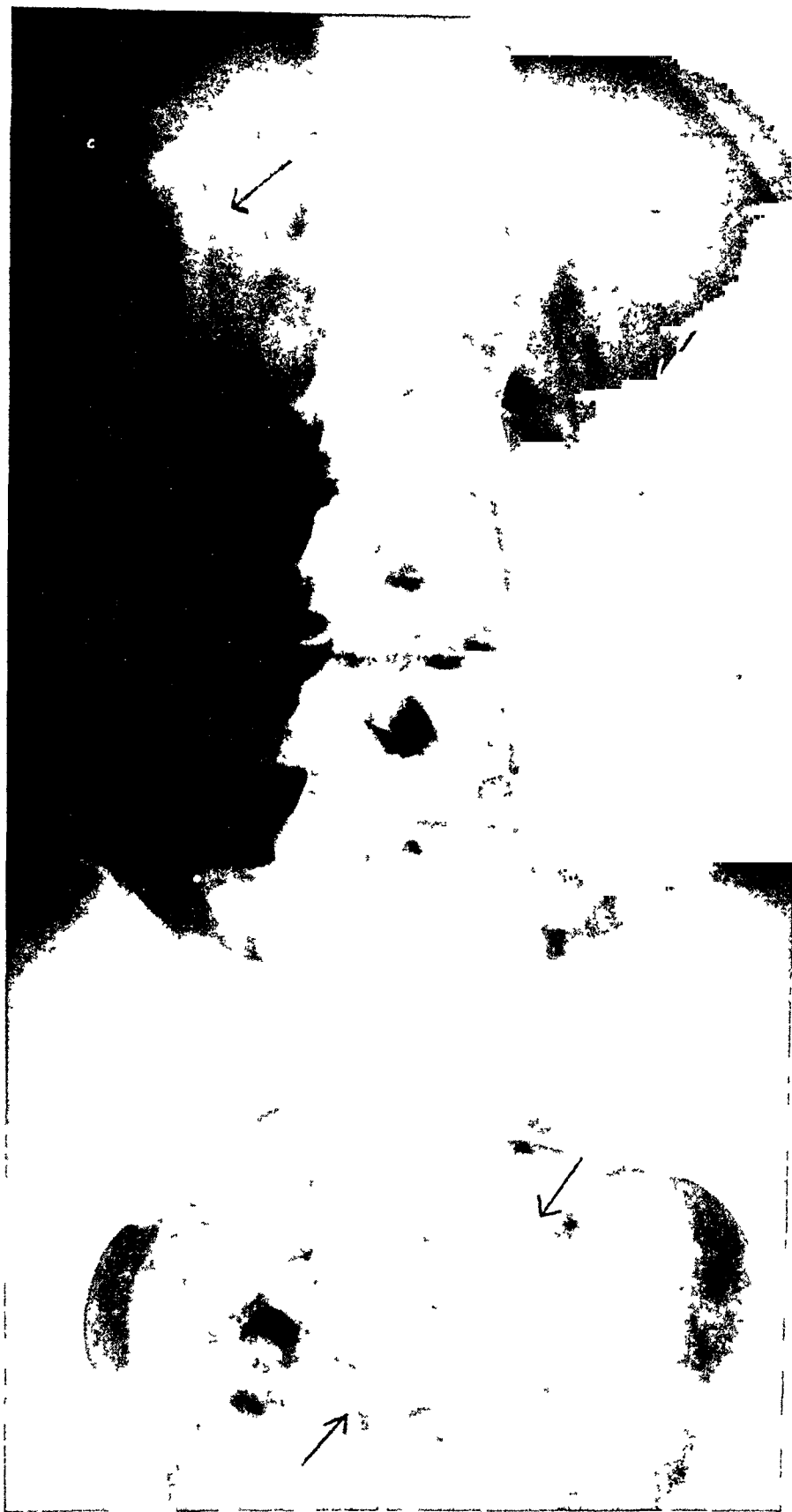


Fig. 3.—Broad shadow concavity in left uterine wall indicating submucous fibroid invading uterine cavity.

menstrual or ovulatory phase, and for a six-month post-partum, and at least a thirty-day postoperative period.

Although indicated for the study of abnormal bleeding, such as menorrhagia, metrorrhagia and staining, the procedure was employed only during the phase of recession of active bleeding.



Fig. 4.—X-ray evidence of renal excretion of viscorayopake showing bilateral ureteral shadows thirty minutes after the final intrauterine injection. Note residual dye in the pelvis.

In the examination of palpable pelvic masses, dysmenorrhea or obscure pelvic pain, additional valuable information was very often made available. This method proved worth while also in determining the structural status of the Fallopian tube, particularly in patients treated for sterility.

Results

Thirty-eight women were x-rayed routinely in the course of sterility studies, after insufflation with the Rubin apparatus and technique had been performed. Numerous interesting and varied uterine anomalies and tumors, as well as unsuspected tubal disease resulting in canal closure and distortion, were found.

Infantile uterus was observed twice: one showed incomplete fusion of the Müllerian ducts (Fig. 5) and the other a cervix four inches long. Bicornuate uterus, and ovarian cyst, respectively, were diagnosed twice. Eight sterility patients had tubes which, although patent, showed marked curling, dilatation and partial obstruction due probably to peritubal adhesions. These conditions, commonly recognized as possible underlying causes of sterility, are very often not detected

on bimanual examination. Their unexpectedly high incidence emphasizes the importance of x-ray as a routine measure to be used in conjunction with the Rubin insufflation test.

Findings by both methods were invariably in agreement, although, in one instance in which a preliminary insufflation indicated tubal closure, x-ray revealed bilateral patency. Moreover, in another instance, a repeated hystrogram disproved cornual obstruction observed in previous x-ray films. On these rare occasions, a physiological contraction or spasm of the uterotubal sphincter muscle may take place,²¹ and a conclusive prognosis therefore should be reserved until at least several confirmatory x-ray studies have been made.



Fig. 5.—Bicornuate uterus and one patent tube demonstrated by viscorayopake.

Among thirty-eight sterility studies, tubal patency in one or both tubes was demonstrated twenty-seven times. In fifteen instances, both tubes were open, but in eight of these women, there were varying degrees of kinking and dilatation. In twelve patients, only one tube was visualized as patent. Among these, there were four postoperative cases in which the unilateral absence in x-ray films was verified by reports of salpingectomy received from the attending surgeons: in one of these a short tubal stump was visualized. In the remaining eight in-

stances of unilateral obstruction, five occurred proximally, two centrally, and one at the distal end (Fig. 6).

Bilateral closure occurred at the fimbriated portion in three instances, centrally in two, and proximally, at the uterotubal junction in six instances. Of the latter, three must be assumed to have been patent, since x-rays were unwittingly taken during already existing pregnancies. Two of these women, with long-standing amenorrhea, had been previously insufflated, and were six weeks gravid (Fig. 7), while the third was an obese, eight-month amenorrheic patient of menopause age (44 years), in whom an eighteen-week fetus was revealed on x-ray. All three gravidities continued uninterruptedly and were delivered at term of normal babies. The constancy in x-ray of cornual closure in all three gravidities gave rise to the query as to whether uterine gestation affects, or coexists with a physiological contraction of the uterotubal muscle.



FIG. 6.—Extrapelvic ovarian cyst diagnosed by presence of displaced course of Fallopian tube shadow.

Pathologic findings, predetermined correctly in most instances by pelvic examinations, were also studied by radiography in the remaining fourteen patients. In each case, further knowledge was obtained, and, several times, planned surgical procedures were changed because of the x-ray findings. The stereoscopic technique proved valuable in determining not only the exact position but the relative size of the tumors.

There were six fibroids, four ovarian tumors, two hydrosalpinx (Fig. 8), one uterine polyp and one multiple carcinoma of the uterus and tube. Menometrorrhagia was the chief complaint in all these women.

There were four submucous fibroids (Fig. 3) and two cases of fibroid uteri in which the cavity was not invaded. Tubal displacement characterized the latter films.

Two ovarian cysts were intraligamentous, and in one instance, in which the diagnosis of a "large subserous fundal fibroid" was made at another hospital, our x-ray findings (Fig. 6) revealed a unilateral ascending linear shadow, which corresponded to the canal of the tube displaced cephalad by an extrapelvic ovarian tumor. The histologic report was serous cystadenoma of the ovary.



Fig. 7.—Hysterogram of clinically unrecognized early pregnancy showing bilateral obstruction at the uterotubal sites.

In both cases of hydrosalpinx, the x-ray findings were more clearly diagnostic than bimanual pelvic examinations.

At curettage, a small clinically unrecognized uterine polyp, causing menopausal bleeding was removed after hysterogram revealed its presence.

In an obese, sixty-two-year-old woman, with metrorrhagia, discharged recently from another hospital with a diagnosis of "abdominal tumor, inoperable," hystero-graphy revealed a double lesion, namely, a uterine carcinoma, and an abnormally large intra- and extrapelvic tubal shadow, which, at operation, was found to be a huge tubal carcinoma. Here, preoperatively, the otherwise unrecognizable pelvic origin of an abdominal mass was ascertained.



Fig. 8.—Hysterosalpingogram showing bilateral pyosalpinges in a sterility patient.

Conclusion

1. Viscorayopake, a recently introduced opaque fluid, has proved eminently satisfactory for clinical use in x-ray study of the female genitalia.

2. Hysterosalpingography was employed in fifty-two patients with gynecological disorders. These included pelvic tumors, pain, uterine bleeding, dysmenorrhea and sterility. In the sterility studies, it proved valuable in conjunction with the Rubin insufflation test.

3. Information as to the size, location and type of intra- and extra-uterine growths, as well as the structure and patency of the Fallopian tube, was obtained. The x-ray differentiation between uterine and

ovarian tumors, as well as abdominal and pelvic growths, was of noteworthy diagnostic significance. The high incidence of unsuspected lesions in sterility studies was remarkable.

4. The facility and safety of the technique and the simplicity of the x-ray film interpretation warrant its use as a diagnostic routine measure in both hospital and office.

5. The technique for the test is described. Contraindications and indications for its use and the advantages and pitfalls inherent in the procedure are noted. Clinical sequelae are also mentioned.

6. The constant x-ray evidence of tubal closure in three pregnant patients may indicate that a uterotubal sphincter spasm occurs physiologically in the gestational state.

7. Findings are statistically presented with reproductions of interesting x-ray films.

8. A brief history of hystero-graphy is included.

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VALIDITY OF TWO-HOUR RAT TEST FOR HUMAN PREGNANCY*

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TWO biologic tests for the determination of early pregnancy have come into general use, the Aschheim-Zondek (mouse test) and the Friedman modification (rabbit). The accuracy of these tests is very good, but the length of time required of 96 and 36 hours, respectively, is one of the drawbacks. Frank and Berman¹ described a 24-hour pregnancy test, using rats; Crew² and Weisman, Snyder and Coates³ published procedures using *Xenopus laevis* (toad) for pregnancy diagnosis in which results were obtainable within 4 to 18 hours. Later in 1942, U. J. Salmon, S. H. Geist, A. A. Salmon and I. L. Frank⁴ published an interesting paper describing a six-hour pregnancy test using immature rats, and subsequently published an abstract⁵ stating 96 per cent accurate results were obtainable within two hours.

The test described by Salmon, et al.,⁵ seemed to satisfy the needs for a practical, rapid test, so we endeavored to determine the reliability of the two-hour rat test for ascertaining human pregnancy.

A series of tests was performed on urine samples as follows:

1. For pregnancy diagnosis
2. For known conditions of nonpregnancy

Our findings showed the test to be not only positive for conditions of pregnancy, but also for women undergoing menopausal changes, for women at midmonth primarily, for males anticipating coitus, and male and female subjects after coitus.

Material and Methods

Over 360 urine specimens were tested on over 1,000 immature female Wistar albino rats for color reaction, to determine pregnancy and nonpregnancy conditions. The urines for the pregnancy tests were supplied chiefly through a laboratory specializing in performing the Friedman rabbit test. The results of the Friedman test obtained in the laboratory of Dr. Frederick Langner were compared with the two-hour rat test findings, and clinical diagnosis secured in any cases in which results were doubtful.

We used the two-hour rat test described by Salmon et al., in most instances, and repeated occasionally with the four- to six- or twenty-four-hour test. A hooded strain of rats was also tested, but the ovaries showed normally positive pink to red color without treatment of any sort, and therefore this strain was discarded as unsatisfactory. For the test, at least two immature female Wistar albino rats of known age and weight (ages 22 to 33 days, and 30 through 45 grams) were each

*This investigation was aided by a grant from the Samuel S. Fels Fund.

injected subcutaneously with 2 c.c. of specimen of urine. At the end of the desired hour, the rats were gassed individually in a closed chamber for about two and one-half minutes, until dead, and the ovaries exposed and examined. The ovary was usually lifted out of the abdominal cavity by means of a small hook, to avoid changes in circulation. Negative ovaries appeared uniformly pale and cream colored. Positive ovaries had a definite blush to strong red color. To eliminate incorrect and impressionistic readings, the ovaries were read promptly upon exposure, then compared with colors on a scale. Satisfactory positive colors were secured for comparison purposes by using a hemoglobin scale (Tallqvist) from 60 per cent up. However, the confusing negative colors could not be identified on the Tallqvist scale, so a simple color scale was designed for reading various negative and positive shades of ovarian reaction, based on the Munsell color chart system.

Results

In Table I is a summary of the tests for diagnosis of conditions of pregnancy. In 61 subjects both the two-hour rat test and the rabbit test were in agreement. There were 46 positive tests for pregnancy, and 15 negative reactions. The rat test was likewise in agreement for the six-hour and twenty-four hour period.

In 11 subjects, with age range of 40 to 56 years, there was practically no agreement between the two-hour rat test and the rabbit test. The two-hour rat test was positive in 11 tests, while the rabbit reaction was negative in 10 of the 11 tests. The clinical diagnosis indicated menopausal difficulties in all cases, and physicians confirmed the diagnosis in all cases at a later date as nonpregnant. The positive reaction in the two-hour rat test often faded to negative in the six and twenty-four-hour tests.

In eight other subjects, with age range of 19 through 46 years, there was a marked disagreement in the results of the two-hour rat test and the rabbit test. Nine of the two-hour rat tests were positive, while only one of nine tests was positive for the rabbit test. The clinical diagnosis proved the two-hour rat test to be more accurate in these subjects, for six of the subjects were pregnant and one not pregnant. One of the subjects was diagnosed as insane, and was not pregnant. The two-hour rat test was apparently more sensitive than the rabbit test, for several of the same subject's specimens became positive when repeated on samples secured approximately a week later. This was further confirmed by the fact that a known pregnancy of day age 41 proved definitely positive in the two-hour rat test and only weakly positive in the rabbit test. On day 44, a specimen from the same woman was read as only moderately positive in the rabbit test.

Male urine served frequently for control injections, and on one particular occasion it was observed the specimen was markedly positive in reaction, an unusual occurrence. It was finally determined the only factor that could explain the change was coitus the previous evening. This observation was confirmed, and suggested a series of studies on color reactions accompanying sexual excitement.

In Table II are summarized the results of the reactions accompanying sexual excitement in three male and three female subjects. The 42 male samples tested on 66 rats (the two-hour rat test) showed five positive and one negative reaction one hour before anticipated evening coitus. The control specimens secured the morning of the scheduled evening

TABLE I. COLOR TEST FOR PREGNANCY

| TABLE I. COLOR TEST FOR PREGNANCY | | | | | | | | | |
|--|---|----------------|------------------|---------------------|--------------------|------------------|----------------------------|--------------------|--|
| ALL SAMPLES OF UNKNOWN | | | | | | | | | |
| | NO. OF SUBJECTS | NO. OF SAMPLES | NO. OF RAT TESTS | RABBIT TEST RESULTS | RAT TEST RESULTS | | | CLINICAL DIAGNOSIS | |
| | | | | | 2 HOURS | 4 TO 6 HOURS | 24 HOURS | | |
| A. Agreements (with rabbit tests) | 61 (Age 19 to 40 years) | 61 | 78 | 46 Pos. 15 Neg. | 46 Pos. 15 Neg. | 4 Pos. 4 Neg. | 7 Pos. 1 Neg. 2 Pos. | Menopausal | |
| B. Disagreements 1. Menopause | 2 11 (Age 40 to 56 years) | 2 11 | 2 19 | 1 Pos. 10 Neg. | 11 Pos. | 3 Pos. 1 Neg. | 1 Pos. 2 Neg. | | |
| 2. Clinical Diagnosis vs. Laboratory Diagnosis | 7 (Age 19 to 46 years) 1 (Age 38) | 8 1 | 8 1 | 8 Neg Pos. | 8 Pos. Pos. | | | | 3 Pregnant 1 Not pregnant 1 Insane (Not pregnant) |

event showed four positive and eight negative responses. The after-coitus specimens showed four positive and one negative within one hour, eight positive and one negative within four hours, and six positive and five negative within eleven hours.

TABLE II. COLOR TESTS FOR NONPREGNANCY CONDITIONS

| REACTIONS ACCOMPANYING SEXUAL EXCITEMENT | | | | | | |
|--|------------------|------------------|---|----------------------------------|------------------|------------------|
| NO. OF SUBJECTS | NO. OF SAM- PLES | NO. OF RAT TESTS | CONDITION OF EXPERIMENT | RAT TEST RESULTS | | |
| | | | | 2-HOUR | 6-HOUR | 24-HOUR |
| 3 Males | 42 | 66 | Coitus | | | |
| | | | Before (P.M.) | | | |
| | | | Within 1 hour | 5 Pos. 1 Neg. | | 1 Pos. 2 Neg. |
| | | | After | | | |
| | | | Within 1 hour | 4 Pos. 1 Neg. | 1 Pos. | 1 Neg. |
| | | | Within 4 hours | 8 Pos. 1 Neg. | 1 Neg. | 5 Pos. 2 Neg. |
| 3 Males | 11 | 17 | Within 11 hours | 6 Pos. 5 Neg. | | 2 Pos. 3 Neg. |
| | | | Control (A.M.) | 4 Pos. 8 Neg. | | 2 Pos. 3 Neg. |
| 3 Females | 50 | 77 | Coitus | | | |
| | | | Before | | | |
| | | | A.M. | | | |
| | | | (Cycle days 11, 13, 15) | 2 Pos. 1 Neg. | | 1 Pos. |
| | | | (Cycle days 10, 16 to 21) | 2 Pos. 1 Neg. 2 Doubtful | | 1 Pos. |
| | | | Within 1 hour (P.M.) | 1 Pos. | | |
| | | | (Cycle days 11, 12 and 13) | 3 Neg. | | 1 Neg. |
| | | | (Cycle days 9, 23 and 24) | 3 Neg. | | |
| | | | After | | | |
| | | | Within 1 hour | 2 Pos. 2 Neg. | | 1 Pos. 1 Neg. |
| | | | (Cycle days 12, 13, 17 and 23) | | | |
| | | | Within 4 hours | 9 Pos. | 1 Pos. | 4 Pos. 3 Neg. |
| | | | (Cycle days 9, 11 to 13, 15 and 23) | | | |
| | | | Within 11 hours | 10 Pos. 11 Neg. 1 Doubtful | 1 Pos. 1 Neg. | 5 Pos. 7 Neg. |
| | | | (Cycle days 9 to 14, 16, 20, 24 and 25) | | | |

In fifty samples of three females tested on 77 rats, the two-hour rat test showed on the morning of the day of anticipated coitus two positive, four negative, and two doubtful reactions during the safe period (days 9, 10, 16 to 24), and three positive and four negative during unsafe period (days 11, 12, 13 and 15). The aftercoitus specimens showed responses quite similar to the male, namely, two positive and two negative within one hour, nine positive within four hours, and eleven positive, eleven negative and one doubtful within eleven hours. The six and twenty-four-hour rat tests showed that a positive two-hour rat test may remain positive or fade, to become negative.

In Table III are summarized the daily reactions on three complete cycles on samples of three unmarried women. In the 81 samples tested on over 109 rats, there were positive reactions usually three days in succession during the midinterval. Positive reactions occurred also one

TABLE III. COLOR TEST FOR NONPREGNANCY CONDITIONS

| DAILY REACTIONS ON THREE COMPLETE CYCLES | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|----------------------------------|--------------------------------------|--------------------------|-----------------------|---------------------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| | | DAY OF CYCLE (TWO-HOUR RAT TESTS) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| NO. OF SUB- JECTS | NO. OF SAM- PLING CYCLE | NO. OF RAT TESTS | INDI- VIDUAL CYCLE | LENGTH OF CYCLE | SUMMARY OF REACTIONS | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
| 1 | 21 | 36 | N. M. (23 yr.) | 26 | 7 Pos. 17 Neg. | + | 0 | 0 | | | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | | | | |
| 1 | 31 | 34 | E. Y. (31 yr.) | 31 | 9 Pos. 21 Neg. 1 Doubtful | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ? | + | + | |
| 1 | 26 | 39 | J. E. (23 yr.) | 29 | 4 Pos. 22 Neg. | 0 | + | 0 | 0 | 0 | 0 | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| 3 | 81 | 109 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

Note:

Note:

In three complete cycles, there were a total of 12 positive, 60 negative and 1 doubtful reactions on days other than the 9 positives of the midperiod.

Results of 6-hour rat test: 3 Positives in 19 tests.

Results of 24-hour rat test: 1 Positive in 9 tests.

TABLE IV. COLOR TEST FOR NONPREGNANCY CONDITIONS

| REACTIONS DURING MIDPERIOD | | | | DAY OF CYCLE (2-HOUR RAT TEST RESULTS) | | | | | | | | | | | | |
|----------------------------|-------------------|------------------------|----------------------|---|--------|--------|------------------|------------------|------------------|------------------|---------------------------------|------------------|------------------|--------|---|---|
| NO. OF SUBJECTS | NO. OF SAMPLES | NO. OF RAT TESTS | INDI- VIDUAL | LENGTH OF CYCLE | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | | |
| 8 Females | 93 | 124 | N. M. (23 yr.) | 28 | 0 | 0 | 0 | + | + | + | + | 0 | 0 | 0 | | |
| | | | | 26 | 0 | 0 | 0 | | + | + | 0 | 0 | 0 | 0 | | |
| | | | | 32 | 0 | 0 | 0 | | | + | | + | + | 0 | 0 | |
| | | | E. Y. (31 yr.) | 28 | 0 | + | 0 | 0 | 0 | + | + | + | + | + | + | 0 |
| | | | | 31 | 0 | | 0 | 0 | 0 | + | + | + | + | + | 0 | 0 |
| | | | J. E. (23 yr.) | 32 | 0 | 0 | 0 | 0 | + | 0 | + | + | + | 0 | + | 0 |
| | | | | 29 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | 0 | 0 |
| | | | | 29 | 0 | 0 | | | | | | | | | | |
| | | | D. K. (19 yr.) | 42 | | | | 0 | 0 | 0 | 0 | + | + | + | 0 | 0 |
| | | | | 30 | | | | | | | | | | | | |
| | | | H. DeW. (20 yr.) | 32 | | | | | + | + | | + | + | 0 | | |
| | | | L. A. F. (34 yr.) | 31 | | | | | | + | 0 | 0 | 0 | | | |
| | | | D. T. T. (28 yr.) | 29 | | | 0 | 0 | 0 | 0 | + | 0 | | | | |
| | | | E. F. M. (26 yr.) | | | | | | | | | | | | | |
| | | | | 31 days ave. | 3 Neg. | 6 Neg. | 1 Pos. 6 Neg. | 2 Pos. 7 Neg. | 5 Pos. 7 Neg. | 8 Pos. 6 Neg. | 10 Pos. 2 Neg. 1 Doubtful | 5 Pos. 8 Neg. | 3 Pos. 6 Neg. | 7 Neg. | | |

Results of 6-hour rat test: 3 Pos.
19 Neg.24-hour rat test: 1 Pos.
8 Neg.(Miss E. H., Aged 24) Pos. (Cycle days 15 to 17
(Subject abnormal receiving medical
treatment.) 19 to 23)

day during menstruation, as well as late in the cycle. The positive two-hour rat test has great tendency to fade if read at six or twenty-four hours.

In Table IV are summarized reactions during midperiod of the cycles in eight women. In the fourteen cycles that averaged 31 days in length, the 93 samples tested on 124 rats showed positive reactions usually for three successive days, the greater number occurring on days 14, 15, 16 and 17, with range of days 12 through 18. The two-hour positive reaction has great tendency to fade out to negative during the six and twenty-four-hour tests in the midperiod samples.

Discussion

It is unfortunate that the two-hour rat test proved positive in conditions other than pregnancy. For individuals up to thirty-seven years of age, the two-hour rat test may prove satisfactory for pregnancy diagnosis, but it would be advisable, when reactions are relatively weak, to confirm with the 24-hour rat test.

The two-hour rat test, when used with the color scale, offers new possibilities for indication of hormone output. The test has been used with some success for establishing probable time of ovulation for insemination purposes. In Table IV one subject (D. T. T.) had only a single positive reaction at midperiod interval, rather than the usual three positive days. This subject has to date been unable to conceive successfully, in contrast to some others tested, and this finding suggests the lack of the hormone essential in normal process of ovulation.

Table III indicates women are cyclic in nature, as determined by occurrence of positive reactions during midperiod interval, during menstruation, and again late in the cycle. Farris⁶ reported a cyclic pattern of activity in women, with a definite increase in walking at the three periods of the cycle, when the two-hour rat test became positive. In contrast, the male is noncyclic, and is apparently stimulated to produce sufficient hormone to cause a positive reaction even when anticipating coitus.

Table II shows both men and women have positive reactions postcoitus. This finding suggests a possible explanation regarding certain normal couples desirous of having children, without success. The usual sexual history of such couples indicates that coitus occurs much more frequently than in the usual successful couple. Is it possible that the stimulation of frequent coitus produces an excess hormonal output in the female to offset the normal, rhythmical hormonal balance? This theory is being tested.

Summary

The two-hour rat test was not found to be specific for diagnosis of pregnancy.

The two-hour rat test gave positive color reactions in nonpregnancy conditions as follows:

- a. In women undergoing menopausal changes.

- b. In normal women for three successive days during mid-interval of cycle, with range from the twelfth through the eighteenth day.
- c. In normal women on single days, usually during menstruation and again late in cycle.
- d. In men and women after coitus.
- e. In men anticipating coitus.
- f. In one woman with hydatidiform mole.
- g. In one woman with clinical diagnosis of insanity.

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STATUS OF INFANT AT BIRTH AS RELATED TO BASAL METABOLISM OF MOTHER IN PREGNANCY*

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WHAT relationship exists between a woman's basal metabolic rate and the birth weight of her infant? Do disturbances of maternal thyroid function affect the growth pattern of the fetus? How imperative is it that "hypothyroid women" be fed thyroid during pregnancy? Is it possible to control the "obesity" of the fetus by feeding thyroid gland to the mother during pregnancy? These and numerous corollary questions are repeatedly asked and answered in medical literature. Unfortunately, the answers are often equivocal, in some instances definitely conflicting. We shall consider here certain of the controversial questions regarding the relationship of thyroid function during pregnancy to the status of infants at birth and during the first six months of life.

We have very carefully collected, at the Fels Research Institute, several hundred basal metabolism readings in various stages of pregnancy and on the same women in a nonpregnant state. Furthermore, we have extensive data on the physical state of infants of these mothers and on their growth progress for a number of years. In this communication we shall therefore present the results of the examination of this data together with such conclusions as seem warranted.

Method of Study

Basal metabolic rates on 163 women in the last month of pregnancy, as well as data on the gain in basal metabolic rate from the beginning of pregnancy to the ninth month, were used in the present study. All basals were done in duplicate by the indirect method. Only subjects who live within a short radius of the Institute were included, and an adequate pretest rest period was required. Most patients have anywhere from six to twenty-four basals taken here over the course of and following their pregnancies, so that the inaccuracies often encountered as a result of apprehension or poor preparation were largely eliminated. Mothers were divided in groups of "high," "intermediate," and "low" ninth month basals, and "high," "intermediate," and "low" B.M.R. gain during pregnancy.

Measurements and x-rays of infants were made at birth, and subsequent growth and development carefully followed by members of our staff. The following items were used in the present study:

*We wish to express our appreciation for the contribution in terms of data collection and, in some instances, statistical treatment of material by members of the staff, particularly Janet Lipford, Margaret Johnston, and Margaret Anderson.

At Birth: Weight, length and a weight/length cubed index.
 At One Month: Skeletal development (number of ossification centers present in the extremities on the left side).
 At Three Months: Gain in weight, gain in length, and gain in skeletal development.
 At Six Months: Gain in weight, gain in length, and gain in skeletal development.

Differences between infants, on the basis of the above characteristics, were analyzed as follows:

1. Infants of mothers with a low B.M.R. at ninth month of pregnancy were compared with infants of mothers with a high B.M.R. at ninth month of pregnancy.

2. Infants of mothers with a low B.M.R. *gain* during pregnancy were compared with infants of mothers with a high B.M.R. *gain* during pregnancy.

The intermediate groups were disregarded.

The following limits defined a low or a high classification in each category:

1. B.M.R. in Ninth Month of Pregnancy:
 - Low—a B.M.R. of +1 and less (55 cases)
 - High—a B.M.R. of +12 and more (43 cases)
2. Gain in B.M.R. During Pregnancy:
 - Low—a gain of 8 and less (40 cases)
 - High—a gain of 20 and more (43 cases)

In comparing the infants, boys and girls were at first treated separately and then grouped for final analysis, when it was determined that for the present study separate consideration of the sexes did not significantly change the results.

Results

Table I shows a comparison of infants of mothers with low ninth month B.M.R. and infants of mothers with high ninth month B.M.R.

TABLE I. A COMPARISON OF MEAN VALUES FOR VARIOUS PHYSICAL ITEMS. "LOW B.M.R. GROUP" CONTAINS INFANTS OF MOTHERS WITH LOW B.M.R. IN THE NINTH MONTH OF PREGNANCY; "HIGH B.M.R. GROUP" CONTAINS INFANTS OF MOTHERS WITH HIGH B.M.R. AT THIS PERIOD

| | WEIGHT (GM.) | | | HEIGHT (CM.) | | | OSSIFICATION (NO. CENTERS) | | | WT. L ³ |
|---------------------------------|-----------------|-------|-------|-----------------|-------|-------|-------------------------------|-------|-------|-----------------------|
| | BIRTH | GAIN | | BIRTH | GAIN | | 1 MO. | GAIN | | BIRTH |
| | | 3 MO. | 6 MO. | | 3 MO. | 6 MO. | | 3 MO. | 6 MO. | |
| Low B.M.R. group | 3,374 | 2,341 | 4,120 | 50.1 | 9.9 | 16.3 | 4.1 | 2.6 | 5.9 | 271 |
| High B.M.R. group | 3,588 | 2,314 | 4,067 | 50.8 | 10.1 | 16.1 | 4.4 | 2.5 | 5.4 | 272 |
| Difference | 214 | 27 | 53 | 0.7 | 0.2 | 0.2 | 0.3 | 0.1 | 0.5 | 1 |
| Critical ratio of difference | 2.3 | -- | -- | 1.3 | -- | -- | -- | -- | 1.7 | -- |
| Group leading | High | Low | Low | High | High | Low | High | Low | Low | High |

Infants of mothers with high B.M.R. were heavier and longer at birth and more advanced skeletally at one month than infants of mothers with low B.M.R. This difference is statistically significant in the case

of birth weight. Infants of mothers in the low group tended to gain faster in weight, height and ossification during the first six months than did the infants in the high group. There is only a slight difference between the children in the weight/length cubed index at birth, the infants of the high group weighing slightly *more* per unit length.

Table II shows a comparison of children of mothers with a low B.M.R. gain during pregnancy and children of mothers with a high B.M.R. gain during pregnancy.

TABLE II. A COMPARISON OF MEAN VALUES FOR VARIOUS PHYSICAL ITEMS. "LOW B.M.R. GAIN GROUP" CONTAINS INFANTS OF MOTHERS WITH LOW GAIN IN B.M.R. DURING PREGNANCY. "HIGH B.M.R. GAIN GROUP" CONTAINS INFANTS OF MOTHERS WITH HIGH GAIN IN B.M.R. DURING THIS PERIOD

| | WEIGHT (GM.) | | | HEIGHT (CM.) | | | OSSIFICATION (NO. CENTERS) | | | WT. L ³ |
|---------------------------------|-----------------|-------|-------|-----------------|-------|-------|-------------------------------|-------|-------|-----------------------|
| | BIRTH | GAIN | | BIRTH | GAIN | | 1 MO. | GAIN | | BIRTH |
| | | 3 MO. | 6 MO. | | 3 MO. | 6 MO. | | 3 MO. | 6 MO. | |
| Low B.M.R. gain group | 3,268 | 2,336 | 4,205 | 49.6 | 10.1 | 16.7 | 4.1 | 2.6 | 5.6 | 268 |
| High B.M.R. gain group | 3,584 | 2,254 | 4,099 | 50.9 | 9.9 | 16.2 | 4.8 | 2.8 | 5.9 | 274 |
| Difference | 316 | 82 | 106 | 1.3 | 0.2 | 0.5 | 0.7 | 0.2 | 0.3 | 6 |
| Critical ratio of difference | 3.0 | -- | -- | 2.7 | -- | 1.3 | 1.7 | -- | -- | 1.0 |
| Group leading | High | Low | Low | High | Low | Low | High | High | High | High |

Infants of mothers with a high B.M.R. gain were heavier and longer at birth and more advanced skeletally at one month than infants of mothers in the low gain group. These differences are statistically significant in the case of birth weight and birth length. Infants of mothers in the low gain group during pregnancy gain faster in weight and length during the first six months. Rate of gain in ossification in the two groups is almost the same, favoring slightly the high group. The high group has a slightly larger weight/length cubed index, that is, they were heavier per unit length.

TABLE III. A COMPARISON OF MEAN VALUES FOR VARIOUS PHYSICAL ITEMS. "LOW B.M.R.—LOW GAIN GROUP" CONTAINS INFANTS OF MOTHERS WITH BOTH LOW B.M.R. IN THE NINTH MONTH OF PREGNANCY AND LOW GAIN IN B.M.R. DURING PREGNANCY; "HIGH B.M.R.—HIGH GAIN GROUP" CONTAINS INFANTS OF MOTHERS IN THE OPPOSITE CATEGORY

| | WEIGHT (GM.) | | | HEIGHT (CM.) | | | OSSIFICATION (NO. CENTERS) | | | WT. L ³ |
|------------------------------------|-----------------|-------|-------|-----------------|-------|-------|-------------------------------|-------|-------|-----------------------|
| | BIRTH | GAIN | | BIRTH | GAIN | | 1 Mo. | GAIN | | |
| | | 3 Mo. | 6 Mo. | | 3 Mo. | 6 Mo. | | 3 Mo. | 6 Mo. | |
| Low B.M.R.— Low gain group | 3,321 | 2,548 | 4,389 | 49.6 | 10.2 | 16.7 | 3.9 | 2.4 | 5.6 | 271 |
| High B.M.R.— High gain group | 3,652 | 2,401 | 4,197 | 51.3 | 10.0 | 16.2 | 4.6 | 2.6 | 5.3 | 273 |
| Difference | 331 | 147 | 192 | 1.7 | 0.2 | 0.5 | 0.7 | 0.2 | 0.3 | 2 |
| Critical ratio of difference | 2.8 | -- | -- | 2.6 | -- | -- | 1.7 | -- | -- | -- |
| Group leading | High | Low | Low | High | Low | Low | High | High | Low | High |

An examination of our data indicates that the mothers who show a low B.M.R. at ninth month are also in many cases mothers with a low B.M.R. *gain* in pregnancy. The coefficient of correlation (r) between ninth month B.M.R. and the B.M.R. gain is +0.68. It was therefore felt that a selection of infants based on still another low-high comparison might prove interesting. In Table III, the infants of mothers who have both a low B.M.R. in the last month of pregnancy and a low B.M.R. gain during pregnancy are compared to infants who are high in both categories.

This comparison sharpens the differences already presented. The high group is advanced at birth, and heavier per unit length, while the low group tends to gain faster during the first six months. These differences are statistically significant for birth weight and birth length.

Discussion

Arnold,¹ in a preliminary report, suggests with caution that he has "reduced fetal obesity" by feeding pregnant women 3 to 6 grains daily of desiccated thyroid gland throughout gestation. The infants of 116 mothers so treated had a mean weight of 6.8 pounds. While Arnold has no control group for his thyroid treated mothers, it is presumed that the average weight of 6.8 pounds is below that which would be expected in an untreated series. It is, perhaps, unfortunate that he has no length measurements on his infants. If he had, it is possible that he would have found his infants smaller in length as well as weight. If so, we believe it may be assumed that by giving 3 to 6 grains of desiccated thyroid per day to his mothers, he was then dealing with a group with higher than average B.M.R. The comparison of basal rates in our group with the height, weight and other factors of the children is at first glance contradictory to Arnold's findings and conclusions. Perhaps it is justifiable, therefore, to devote a bit of space to a discussion of possible causes for the discrepancy in our observations.

In considering what effect the feeding of thyroid during pregnancy might have upon the weight of the newborn infant, it is well to think for a moment about the results of hypo- and hyperthyroidism in young animals. Kennedy² states, "The results of feeding large amounts of thyroid substance to young animals are manifested chiefly in a diminished rate of growth, hypertrophy of such organs as the suprarenals, heart, liver, pancreas, spleen, testes, ovaries, and in diminished weight. Cessation of feeding of thyroid gland is followed by acceleration in the rate of growth and in disappearance or hypertrophy of the organs." The same author, in discussing thyroidectomy in young animals, says, "In general there is a retardation of growth, evident particularly in the skeleton, and a depression of all physiological functions of the body." It should be evident then that in the young we are dealing with a thyroid effect which is absent in the adult, namely the control of growth. Effect of thyroid upon the weight of an adult may be primarily on the excess storage of fat. Effect of thyroid upon the weight

of a young child or fetus may be primarily upon the infant's total growth, not its formation of adipose store. Arnold in "reducing fetal obesity" by feeding mothers thyroid may very well simply be depressing the growth of the child, just as the growth of any child suffering from hyperthyroidism is depressed. The real nature of this weight reduction would be shown if Arnold had considered birth lengths.

Arnold's basis for using thyroid therapy as a general procedure in pregnancy is that he believes a state of hypothyroidism normally exists during pregnancy. He draws this conclusion despite the commonly accepted finding of a high basal metabolic rate during late pregnancy. His conclusion is based on the fact that he fails to produce signs and symptoms of hyperthyroidism in his pregnant mothers when he administers 3 to 6 gr. of desiccated thyroid per day. Let us consider for a moment the basis for Arnold's interpretation of thyroid activity during pregnancy. It is a well-established fact that there is normally a rise of perhaps 15 per cent in mothers' B.M.R. as term approaches. Rise in B.M.R. in the absence of infection is in general considered evidence of increased thyroid activity. The rise in pregnancy has been attributed by various investigators both to an increase in the thyroid activity of the mother and to the increasing function of the thyroid of the fetus. Palmer,³ et al., and many others have indicated that the fetal thyroid becomes active at a very early stage, and that the fetus undoubtedly supplies most or all of its own thyroid needs; and perhaps upon occasion, some of those of the mother. The increased oxygen consumption in pregnancy, then, while resulting from either increased maternal thyroid activity or from fetal thyroid, probably represents a higher rate of oxygen consumption by the maternal tissues, as well as by the fetal tissues.

Bodansky and Duff⁴ and others, working with animals, have found that there is a much greater tolerance of thyroxin during pregnancy than in a nonpregnant state. Now a large tolerance of thyroid hormone in the nonpregnant state may or may not be considered adequate evidence of the existence of hypothyroidism. Certainly it is highly doubtful whether such a tolerance during pregnancy should be so interpreted. It must be remembered that the altered physiologic state of pregnancy involves many functions, including possibly the development of anti-hormones, and inhibitory actions by other endocrines. Furthermore, unless we are to change our concept of the terms normal and hypo function, "normal thyroid function" during pregnancy must mean to us the thyroid function usually or customarily existing during that state. Hypothyroid function during pregnancy should mean a degree of function distinctly below that *usually existing during pregnancy*. We must be aware also of the possibility of a selective action of excess thyroid hormone on the mother and fetus. Perhaps the mother herself, through antihormone action or other means maintains a broad tolerance for excessive thyroid substance during pregnancy. Does her fetus, how-

ever, develop a similar tolerance or resistance to excess thyroid? Is it not possible that large doses of thyroid may be well tolerated by the mother but that the high blood levels of thyroid hormone such treatment involves might induce in the fetus a state of hyperthyroidism sufficient to depress growth?

How then may we reconcile our findings that mothers with the higher ninth month rates and with the larger B.M.R. gains, have the largest children, with Arnold's findings that feeding large amounts of desiccated thyroid to normal women produces lighter infants. It seems logical that within the *normal range* of thyroid function, a more adequate, a more optimum level of the hormone would exercise its usual physiologic function of promoting growth—in this instance fetal growth. Since we are in the goiter belt, it is reasonable to believe that some of our mothers do not have entirely optimum thyroid function (and perhaps the same conclusion applies to the fetus). Fetuses of such women would not, therefore, be able to exploit their full intrauterine growth potentialities, and would be somewhat smaller than those of mothers with entirely adequate thyroid function. That such is the case is suggested by the results of our study as shown in Tables I, II, and III. The infants of the mothers with lower basals are smaller than those with higher basals. But in addition, the infants of mothers with the lower basals *are actually less obese* as shown by their weight-length relationships, than are those of mothers with higher basals. This fact is important. It may be argued that mothers with larger babies might be expected to have higher basal rates, because of the higher proportionate weight of high oxygen consuming fetal tissue. Such an explanation still would not account for the lower weight-height relationship of the infants of the low B.M.R. group.

One may wonder whether a similar relationship exists between the thyroids of a mother and fetus as exists between pancreas of mother and fetus. It is known that in maternal diabetes, the fetal pancreas hypertrophies and produces a great deal more insulin than normally in an attempt to compensate for the nonfunctioning maternal pancreas. The result is that although this process is never successful in maintaining fetal blood sugar at its normal level, because of the dilution effect of attempting to supply the whole maternal fetal economy with insulin, the fetus as a newborn has an overactive pancreas. If similarly the fetal thyroid developed an abnormally high rate of activity as a result of maternal deficiency, it might or might not be able to supply both organisms adequately, but it might be an overfunctioning gland at birth. Depending upon how soon its function returned to normal levels, this overactive state might retard early neonatal growth, stimulate that growth, or have little effect. Growth rates of infants of the high and low mothers' basal groups are not greatly different. The infants of the low mothers' basal group do, however, in general have slightly more

rapid growth progress than those of the high group in weight, ossification and height.

Summary

The infants of a "normal" group of mothers were divided into two groups according to the basal metabolic rates of the mothers during the ninth month of pregnancy. A similar division was made on the basis of the mothers' B.M.R. gain during pregnancy. In each instance the infants of the high B.M.R. group were compared with the low B.M.R. group in terms of birth weight and length, weight/length cubed index, and number of ossification centers present in the extremities of the left side (at one month), together with the gains in these categories during the first six months of life. Infants of mothers in the high ninth month B.M.R. group were larger and skeletally slightly more mature than infants in the low B.M.R. group. So were infants of mothers with high B.M.R. gains during pregnancy. Infants in both high groups weighed slightly *more* in relation to their lengths, than did the infants of the low groups. There was some tendency for the infants of the low groups to gain slightly more rapidly in weight, height and ossification during the first six months of life.

Conclusions

There is no evidence from our data that higher basal metabolic rates of mothers during pregnancy are effective in producing smaller or less "obese" babies so long as a state of actual hyperthyroidism does not exist. We question the use of thyroid therapy in normal women for the production of less "obese" infants, since we believe that smaller infants are produced by such means only if the therapy is severe enough to depress all fetal growth processes through the creation of a state of actual hyperthyroidism.

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EXPERIMENTAL BASIS FOR THE CHEMOTHERAPY OF TRICHOMONAS VAGINALIS INFESTATIONS. II*

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LABORATORY evaluation of the in vitro killing and inhibiting effect of various chemicals on *Trichomonas vaginalis* offers useful collateral data for clinical studies and suggests new preparations worthy of therapeutic trial. Several investigators have recorded their observations of the ability of various compounds to kill *T. vaginalis*.¹⁻¹³ Differences in technique make comparison of the recorded data difficult. In addition all recorded tests have presumably been made with bacterially contaminated trichomonads. The detrimental effect of bacterial growth on *T. vaginalis* is well known.

Method

A standardized technique for testing the protozoacidal action of chemicals employing bacteria-free *T. vaginalis*¹⁵⁻¹⁶ has been recorded.¹⁴ In summary it consists of introducing a standard number of bacteria-free *T. vaginalis* (400,000) into a standard volume (4 c.c.) of a drug solution containing 25 per cent human serum adjusted to pH 6 with N/1 HCl. A constant temperature of 37° C. is maintained. Subcultures of 2,000 protozoa are removed at intervals of 5 and 10 minutes by pipette and introduced into C.P.L.M.† medium¹⁴ which will initiate growth if as many as ten or even less viable protozoa capable of multiplying are present. Sterile technique is employed throughout.

The effective concentration of the compound in question is arbitrarily given as that which kills in 10 but not in 5 minutes. Failure to multiply in the C.P.L.M. medium is taken as an indication that the protozoa were killed by contact with the medicament. When all the tested compounds are compared in this manner a relative evaluation of their lethal effect is obtained.

Acidified human serum is employed in the test mixture to simulate empirically the high protein and acid content of vaginal discharge which a successful in vivo trichomonacide must overcome.

The chemicals tested include a large number solicited from various commercial sources, whose cooperation in this study is much appreciated. No compound submitted has been omitted from these experiments. In addition, many other chemicals have been tested for reasons of theory or previous clinical trial. A restricted program for the future makes provision for testing the action of many other compounds as well as their growth-inhibiting action. Interested individuals should feel free to submit material for testing to the junior author.

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†C.P.L.M. = cystine, peptone, liver infusion, maltose.

TABLE I. PART A. TRICHOMONACIDAL COMPOUNDS

Summary of experiments testing the killing action of various chemicals on bacteria-free *Trichomonas vaginalis*. All tests were made in 25 per cent acidified human serum against a standard number of organisms (400,000) in a standard volume (4 c.c.)

| COMPOUND TESTED | CONCENTRATION KILLING IN 10 BUT NOT IN 5 MIN. | pH OF TEST MIXTURE |
|--------------------------------------|---|--------------------------|
| Acetic anhydride | 1:400 | 3.92 |
| Acetarson (Stovarsol) | 1:20 | 8.99 |
| Acriflavine hydrochloride | 1:5,200 | |
| Acriflavine-neutral | 1:5,000 | |
| Aerosol | 1:500 | 5.27 |
| Aldarson | 1:140-1:150 | 6.20 |
| Ammonium thiocyanate | 1:250-1:300 | 6.03 |
| Aniline | 1:100-1:125 | 6.72 |
| Arsphenamine | 1:2,100-1:3,400 | 5.3-5.8 |
| Benzoic acid | 1:600 | 4.4 |
| Boric acid | 1:28 (in 90 min.) | 5.6 |
| Butyl alcohol | 1:40 | 6.3 |
| Butyric acid | 1:250-1:260 | 3.94 |
| Cadmium chloride | 1:900 | 5.58 |
| Caprylic acid | 1:900-1:1,000 | 5.0 |
| Caprylic alcohol | 1:500-1:600 | 5.99 |
| Chloroform | 1:300-1:400* | 6.02 |
| Chromium trioxide | 1:1,000-1:1,100 | 4.33 |
| Citric acid | 1:60 | 2.29 |
| Colloidal chlorothymol | 1:2,200 | 6.28 |
| Cresol-compound solution | 1:400-1:500 | 6.66 |
| Cresylic acid | 1:500 | 6.11 |
| Cupric sulfate | 1:1,100 | 4.9 |
| Dihexylin, aqueous | 1:5,800 | 3.64 |
| Dihexylin, tincture | 1:5,500-1:6,000 | 5.00 |
| Emetine hydrochloride | 1:36 | 5.7 |
| Ethyl alcohol | 9.5-14.25% | 6.32 |
| Ethylhydrocupreine hydrochloride | 1:142 (in 45 min.) | 4.82 |
| Ethyl mercuric chloride | 1:42,000 | 6.3 |
| Floraquin | 70% saturated (in 30 min.) | 5.4-5.8 |
| Formaldehyde | 1:400 | 6.16 |
| Formic acid | 1:500 | 4.12 |
| Fumaric acid | 1:300-1:400 | 3.37-3.9 |
| Gentian violet | 1:1,400-1:1,500 | 6.2 |
| Glycerin | 25%-30% | 6.8 |
| Green soap | 1:400-1:450 | 7.14 |
| Hexylresorcinol | Excess in emulsion | 6.01 |
| Hydrobromic acid | 1:250-1:300 | 2.22-2.68 |
| Hydriodic acid | 1:400-1:450 | 3.43 |
| Isomamyl hydrocupreine hydrochloride | 1:250 | 5.3 |
| Lactic acid | 1:212-1:255 | 3.4-3.5 |
| Lead acetate | 1:100 | 5.8 |
| Levulinic acid | 1:150-1:175 | 3.88 |
| Malachite green | 1:2,000 | 5.3 |
| Maleic acid | 1:250 | 3.02 |
| Malonic acid | 1:200-1:300 | 3.1-3.42 |
| Mandelic acid | 1:350 | 3.95 |
| Mercuric bromide | 1:15,000 | 6.4 |
| Mercuric chloride | 1:23,000 | 6.4 |
| Mercuric oxycyanide | 1:7,200-1:7,700 | 6.1 |
| Mercurochrome | 1:890 | 6.75 |
| Merthiolate | 1:12,000 | 6.7 |
| Methyl alcohol | 15%-20% | 6.5 |
| Methyl violet 6B | 1:5,000 | 6.5 |
| Monochloroacetic acid | 1:900 | 4.2 |
| N-benzoylsulfanilamide | 10% saturated | 10.2 |
| Negaton | 1:120-1:140 | 1.76-2.69 |

*Approximate.

TABLE I—CONT'D

| COMPOUND TESTED | CONCENTRATION KILLING IN 10 BUT NOT IN 5 MIN. | pH OF TEST MIXTURE |
|---|---|--------------------------|
| Neoarsphenamine | 1:2,000 | 6.12 |
| N1-furfurylsulfanilamide | 8% saturated | 10.7 |
| Oxalic acid | 1:300-1:400 | 3.4-3.55 |
| Oxyquinoline sulfate | 1:150-1:175 | 4.30-4.37 |
| Phemerol | 1:1,600 | 5.98 |
| Phenol | 1:210 | 5.9-6.2 |
| Phenyl mercury derivative of p-amino-benzene sulfanilamide | 1:24,000-1:26,000 | 6.4 |
| Phenylmercuric acetate | 1:40,000 | 5.81 |
| Phenylmercuric benzoate | 1:36,000-1:38,000 | 5.8-6.0 |
| Phenylmercuric chloride | 1:34,000-1:38,000 | 5.8-6.0 |
| Phenylmercuric nitrate | 1:36,000-1:38,000 | 5.8 |
| Phosphoric acid | 1:200 | 1.98 |
| Picric acid | 1:400-1:500 | 4.5 |
| Potassium chromate | 1:100 | 7.37 |
| Potassium dichromate | 1:400 | 5.8 |
| Proflavine | 1:4,400-1:4,600 | 6.1 |
| Propionic acid | 1:200-1:250 | 3.96-4.02 |
| Propylene glycol | 20-25% | 6.1 |
| Pyrogallie acid | 1:60-1:80 | 5.85 |
| Pyroligneous acid | 1:20-1:30 | 3.87-4.08 |
| Quinine hydrochloride | 1:100 | 6.3 |
| Saponin | 1:200 | 6.27 |
| Salicylic acid | 2.1-1.1 saturated solution | |
| Saponified castor oil | 1:600 | 6.85 |
| Selenium oxide | 1:350-1:400 | 3.02-3.18 |
| Silver nitrate | 1:28,000-1:30,000 | 6.3 |
| Silver picrate | 1:14,000-1:17,000 | 6.08-6.13 |
| Sodium carbonate | 1:100-1:120 | 9.97 |
| Sod. cobalti nitrite | 1:400-1:500 | 5.02-5.19 |
| Sod. nitroferrie cyanide | 1:250-1:300 | 6.0 |
| Strong silver protein | 1:1,300-1:1,400 | 6.2 |
| Succinic acid | 1:140 | 3.57 |
| Sulfanilylacetanidine | 1:400 | 10.05 |
| Sulfanilamidothymol | 1:250 | 10.29 |
| Sulfarsphenamine | 1:3,000-1:4,000 | 6.0-6.2 |
| Sulfosalicylic acid | 1:150-1:200 | 2.27-2.72 |
| Superoxyl | 1:60-1:80 | 5.0 |
| Tartar emetic | 1:1,600-1:2,000 | 5.63-6.0 |
| Tartaric acid | 1:60-1:80 | 2.33-2.46 |
| Thiobismol | 1:200-1:300 | 6.9-7.32 |
| Trichloracetic acid | 1:400 | 3.2 |
| Triethanolamine | 1:20 | 9.78 |
| Tryparsamide | 1:175 | 6.30 |
| Uranium acetate | 1:200* | 4.66 |
| Valeric acid | 1:250-1:300 | 4.1 |
| Vioform | 70% saturated or 10% Emulsion | 6.3 |
| Vuzin dihydrochloride | 1:2,000 | 5.81 |
| Zinc acetate | 1:140 (in 45 min.) | 5.22 |

Results

The data obtained to the present are tabulated as follows: Table I lists those compounds which exhibit trichomonacidal activity and Table II includes those which failed to kill *T. vaginalis* in vitro within 10 minutes under the experimental conditions employed. Table III summarizes the work done on jellies.

TABLE II. INACTIVE COMPOUNDS

Summary of experiments in which the compounds tested did not kill the standard dose of *T. vaginalis* in ten minutes in the highest concentration tested.

In exploration of many nonproprietary compounds, it was considered impractical to test solutions of higher concentrations than 1:100, since the purpose of the study was to discover substances of greater activity than those now in use. The upper level of concentration was limited in other instances by: (a) the solubility of the compound in question, (b) the concentration of a stock solution as supplied by the manufacturer, (c) dilution resulting from the addition of serum.

| COMPOUND TESTED | HIGHEST CONCENTRATION TESTED | pH OF TEST MIXTURE |
|---------------------------|------------------------------------|--------------------------|
| Acetaldehyde | 1:20 | 4.48 |
| Acid fuchsin | 1:133 | 4.8 |
| Alizarin | 3:1 saturated | 6.58 |
| Alloxan | 1:100 | 3.5 |
| Aluminum amm. sulfate | 1:20 | 3.4 |
| Aluminum chloride | 1:100 | 3.44 |
| Aluminum pot. sulfate | 1:20 | |
| p-amino dimethyl | 1:133 | 4.77 |
| Aniline monohydrochloride | | |
| Ammonium acetate | 1:20 | 5.99 |
| Ammonium bromide | 1:20 | 6.36 |
| Ammonium chloride | 1:20 | 6.18 |
| Ammonium oxalate | 1:100 | |
| Aseptoform-p | 3:1 saturated solution | 6.26 |
| Basic fuchsin | 1:133 | 5.94 |
| Biebrich scarlet | 3:1 saturated | 7.14 |
| Brilliant cresyl blue | 3:1 saturated | 4.12 |
| Carbarsone | 1:100 | 7.79 |
| Carbon tetrachloride | 0.375% | 6.4 |
| Carbon bisulfide | 0.075% | |
| Chiniofon | 1:70 | 6.2 |
| Cotton blue | 1:133 | 5.96 |
| Cresol red | 3:1 saturated | 6.04 |
| Devegan | 70% saturated | |
| Dichloramine T. | 3:1 saturated | 6.31 |
| Diethylene glycol | 1:20 | 6.73 |
| Diphenylamine | 3:1 saturated | |
| Eosin Y | 1.5% | 7.0 |
| Ethyl ether | 3.75% | 6.67 |
| Ferric amm. sulfate | 1:400 | 4.21 |
| Ferrous amm. sulfate | 1:20 | 4.89 |
| Formamide | 1:20 | 6.46 |
| Gallic acid | 1:133 | 3.91 |
| Glycerol phosphate | 1:100 | 7.45 |
| Hippuric acid | 3:1 saturated | |
| Iodoform | 70% saturated | 6.5 |
| Iso-amyllic alcohol | 1:100 | |
| Janus green B | 1:133 | 5.5 |
| Lactose | 11.25% | 7.06 |
| Lenigallol | 10% suspension | 5.1 |
| Lithium carbonate | 1:266 | |
| Lithium lactate | 1:133 | |
| Manganous sulfate | 1:100 | |
| Magnesium sulfate | 1:5 | 6.01 |
| Malic acid | 1:40 | 2.37 |
| Metacine | 6% suspension | 3.11 |
| Methyl orange | 3:1 saturated | 7.2 |
| Methyl red | 3:1 saturated | 5.36 |
| Methylene blue | 1:40 | |
| Naphthylamine | 3:1 saturated | |
| Neutral red | 3:1 saturated | 5.03 |
| Nigrosin | 3:1 saturated | 7.68 |
| Oleic acid | 0.75% | 6.45 |
| Phenol red | 1:133 | 3.9 |

TABLE II—CONT'D

| COMPOUND TESTED | HIGHEST CONCENTRATION TESTED | pH OF TEST MIXTURE |
|--|------------------------------------|--------------------------|
| Phthalic acid | 1:100 | 4.16 |
| Picramic acid | 3:1 saturated | 6.16 |
| Potassium acid phthalate | 1:100 | 4.22 |
| Potassium bromate | 1:100 | 6.2 |
| Potassium chlorate | 1:133 | 6.53 |
| Potassium ferrieyanide | 1:100 | 6.15 |
| Potassium ferrocyanide | 1:20 | 6.42 |
| Potassium iodide | 1:20 | 6.78 |
| Potassium permanganate | 1:100 | 8.34 |
| Potassium persulfate | 1:133 | 4.18 |
| Propyl ester of parahydroxy benzoic acid | 3:1 saturated | 6.26 |
| Pulvis alkalinus fungi | 70% saturated | 8.82 |
| Quinine sulfate | 1:1,000 | 5.43 |
| Red mercuric iodide | 3:1 saturated | 6.6 |
| Red mercuric oxide | 3:1 saturated | 6.68 |
| Safranin | 1:133 | 6.68 |
| Sodium acetate | 1:100 | 6.47 |
| Sodium alizarin sulfonate | 1:133 | 4.93 |
| Sodium anthraquinonesulfonate | 1:140 | 6.1 |
| Sodium barbital | 1:100 | 8.4 |
| Sodium benzoate | 1:100 | 6.31 |
| Sodium bicarbonate | saturated | 8.47 |
| Sodium 2-5-bisulfanilamido- benzenesulfonate | 1:1,000 | 5.6 |
| Sodium borate | 1:100 | 8.77 |
| Sodium bromide | 1:100 | 6.18 |
| Sodium N ¹ -cinnamoyl- sulfanilamide | 1:1,000 | 5.80 |
| Sodium hyposulfite | 1:100 | 5.5 |
| Sodium molybdate | 1:100 | 6.47 |
| Sodium oxalate | 1:100 | 6.78 |
| Sodium pyrophosphate | 1:100 | 8.0 |
| Sodium sulfite | 1:100 | 7.82 |
| Sodium thiocyanate | 1:100 | 6.3 |
| Sodium thiosulfate | 1:100 | 6.23 |
| Sulfanilic acid | 1:133 | 3.12 |
| Sulfadiazine | 1:14,000 | |
| Sulfaguanidine | 1:750 | 5.5-6.0 |
| Sulfamethyldiazine | 1:4,700 | 5.5 |
| Sulfanilamide | 1:178 | 5.8 |
| Sulfapyridine | 1:3,500 | 5.4 |
| Sulfathiazole | 1:1,100 | 5.57 |
| Sulfathiazole and Beta lactose | 70% saturated | 5.69 |
| Tannic acid | 1:20 | |
| Thymol | 1:1,250 | 6.31 |
| Toluol | 1:200 | 6.14 |
| Zephiran | 1:1,400 | 6.2 |
| Zinc acetate | 1:100 | 5.7 |
| Zinc chloride | 1:133 | 5.3 |

Comments

1. Three to one saturated = 3 parts of a saturated (aqueous) solution and 1 part of 100 per cent serum.

2. Potassium permanganate in a concentration of more than 1 per cent forms a solid with the serum. The technique employed in these experiments does not give a fair evaluation of the trichomonacidal effect of the compound.

3. Ferric Amm. sulfate forms a solid with serum in concentrations greater than 0.25 per cent and cannot be adequately tested.

4. Superoxyl decomposes before a test can be completed. This is not a true evaluation of its activity.

Conclusions

1. There are many chemicals which are active trichomonacides in vitro in the presence of acidified 25 per cent human serum.

2. Many of these are so much more active than some commonly employed therapeutic preparations that clinical evaluation of their in vivo effectiveness when incorporated in a suitable vehicle such as a jelly is warranted.

3. Those compounds which were found to kill *T. vaginalis* in a dilution of 1:1,000 or more by the technique employed include:

| | |
|---------------------------|---|
| Acriflavine hydrochloride | Phemerol |
| Acriflavine neutral | Phenyl mercury derivative of p-amino benzene sulfonamide |
| Arsphenamine | Phenylmercuric acetate |
| Caprylic acid | Phenylmercuric benzoate |
| Chromium trioxide | Phenylmercuric chloride |
| Cupric sulfate | Phenylmercuric nitrate |
| Dihexylin | Proflavine |
| Ethylmercuric chloride | Silver nitrate |
| Gentian violet | Silver picrate |
| Malachite green | Strong silver protein |
| Mercuric bromide | Sulfarsphenamine |
| Mercuric chloride | Tartar emetic |
| Mercuric oxycyanide | Vuzindihydrochloride |
| Merthiolate | |
| Methyl violet 6B | |
| Neoarsphenamine | |

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SALMONELLA CHOLERAESUIS BACTEREMIA DURING PREGNANCY

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EVIDENCE at hand indicates that *Salmonella* infections in man are definitely more common than typhoid fever at the present time in the northeastern part of the United States. Typhoid fever is a well-known complication of pregnancy and during the last 40 years, a number of articles have been published on this subject. In contrast, *Salmonella* infection in pregnancy seems to be a very unusual occurrence. A search through the *Quarterly Cumulative Index Medicus* of the last 10 years failed to reveal a single reference, and the Editor of the *Journal of the American Medical Association* states that "we have found no reference, whatsoever, to *Salmonella* infections during pregnancy." It seems to be of interest, therefore, to report here the clinical, bacteriological, and serological findings in a case of *Salmonella choleraesuis bacteremia* in pregnancy.

Report of a Case

Mrs. E. B., aged 24, was admitted to this hospital on November 24, 1943 with a diagnosis of toxemia of pregnancy. The date of the last normal menstrual period was April 25, 1943; that of expected confinement, February 2, 1944. The prenatal period was uneventful until 2 weeks prior to admission when it was found that her blood pressure had risen to 180/120 mm. Hg and her urine showed 4+ albumin. No other symptoms of toxemia were present. Concern over her condition was warranted particularly since a 6 months' pregnancy was terminated in March, 1942 because of high blood pressure and albuminuria. No further observations were made on the blood pressure until the present pregnancy. Her past history was essentially negative except for measles in childhood.

The patient was a short, obese female of Italian birth. The positive findings on physical examination were uterine enlargement of approximately 7 months' pregnancy and edema of the abdominal wall and legs. Fetal heart sounds were not heard, but the patient insisted that she felt life. The blood pressure was 180/110 mm. Hg; the urine showed 4+ albumin, some hyaline casts being present. A diagnosis of recurring toxemia was made. The patient was placed on a salt-free diet and fluids.

Severe epigastric pain requiring morphine occurred over a period of several nights. It was felt that these attacks were not the result of toxemia and other causes were considered. Roentgen-ray examination of the gall bladder was negative. Her temperature and pulse remained normal. Five days after admission, she required treatment for nasal bleeding which originated in a small eroded vessel. Her fluid intake and

output were satisfactory. Following the use of veratrone, the blood pressure was reduced to approximately 150/100 mm. Hg.

Seven days after admission (December 1), the patient had a chill and the temperature rose to 101° F. Physical examination was essentially negative. On the following day a second chill occurred with a temperature rise to 102° F. At that time the patient complained of pain in the right costovertebral angle and stated that she no longer felt fetal movements. Sulfathiazole (7.5 grains every 4 hours) was given for two days. The temperature remained elevated for 3 more days, fluctuating between 98.5° F., and 103° F. The pulse rate varied between 84 and 94 per minute. The systolic blood pressure ranged between 130 and 150 mm. Hg and the diastolic between 80 and 90 mm. Hg. On December 5, the blood culture, taken on December 3, was reported to be positive for paratyphoid bacillus and, consequently, the patient was transferred to the building for contagious diseases. On December 6 and 7, the temperature was normal. However, on December 8, the temperature rose to 102° F. and remained elevated until December 15, ranging between 100° F. and 103.6° F. On December 10, the patient went into spontaneous labor and was delivered of a macerated female fetus. On the first day post partum, the patient had another chill and the temperature rose to 103.6° F. Except for a slight rise of temperature to 100.2° F. on the third day post partum, the temperature remained normal until her discharge on December 20, the twenty-sixth day of hospitalization.

Results of Laboratory Investigations

The pertinent laboratory findings were as follows: During the entire period of hospitalization the urine of the patient contained albumin. Sugar was not present. A few red and white blood cells were seen in the majority of specimens. Occasionally, hyaline and granular casts were present.

A blood count taken on December 4, showed the following: 11 grams of hemoglobin; 3,100,000 red blood cells; 7,800 white blood cells; 67 per cent polymorphonuclear cells, 12 per cent band forms, 18 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophiles. On December 17, the hemoglobin was 8.5 grams and the leucocyte count 6,000. On December 20, the hemoglobin was 9.5 grams. The patient's blood was Rh positive.

Since the cause of the fever remained undetermined, a blood culture was taken on December 3. It revealed the presence of gram-negative bacilli, subsequently identified as *S. choleraesuis*. This organism is also referred to in the literature as *S. suipestifer*. On December 9, another blood culture was taken and again paratyphoid bacilli were recovered; there were 3 colonies per cubic centimeter of blood. The blood culture obtained on December 7, remained sterile.

In order to determine the possible portal of entry, a throat culture was taken on December 8, and the feces were cultured on December 9. Both cultures failed to reveal the presence of paratyphoid bacilli. It is interesting to note that stool specimens taken on December 9, 10, 13, and 15 likewise did not contain *Salmonella choleraesuis*. However, a stool specimen obtained on December 17 (18 days after the onset of the fever) showed paratyphoid bacilli on culture. On the same day the urine was positive for *S. choleraesuis*.

The antibody response of the patient was investigated and the following results were obtained. Blood serum was examined for the presence of agglutinins against stock strains of typhoid and paratyphoid bacilli, *B. proteus* OX₁₀ and *B. abortus*. In addition, the strain isolated from the blood of the patient was used as antigen. The serum of the patient obtained on December 9, failed to agglutinate any of these organisms even when used in a dilution of 1:10. Two days later agglutinins against paratyphoid bacillus appeared. The titer against the stock strain of *B. paratyphosus* and the homologous strain was 1:320 and 1:640, respectively. Twenty-four hours later, December 12, the agglutinin titer against the patient's own strain was 1:2,560. It is evident, therefore, that the patient developed specific antibodies in high titer against *S. choleraesuis*. In this connection it may be pointed out that some authors, for instance, Wing and Tropoli,¹ interpreted the presence of antibodies in titer of 1:80 as indicative of antibody formation. Such a conclusion is not warranted unless it can be shown that the antibody titer increased during or following the infection and is definitely beyond the titer of normal agglutinins.

As previously mentioned, a macerated fetus was delivered on December 10, 1943. It should be noted that at that time the patient's temperature reached 103.6° F., and that, on the day before, the blood culture was positive for *S. choleraesuis*. Bacteriologic studies were carried out on both the fetus and the placenta in order to determine whether or not intrauterine transmission of the paratyphoid bacilli had taken place. The following are the results obtained: The culture taken from the aseptically opened placenta revealed the presence of numerous gram-negative bacilli, subsequently identified as *S. choleraesuis*. Cultures of the heart's blood and mouth of the fetus remained entirely sterile. Thus, it is obvious that, although the organisms were present in the placenta, they had not invaded the blood stream of the fetus.

The placenta was examined by Dr. Kornel L. Terplan who reported these findings:

The placenta measured 13.5 cm. in diameter and 1 to 3 cm. in thickness. There were numerous anemic infarcts. Histologically, considerable autolytic changes with marked leucocytic infiltration of autolytic and necrobiotic areas and with autolysis of the exudate itself were noted. In the areas in which the placental structure was well preserved, these exudative changes were not seen. A few white infarcts with minimal inflammatory changes were present. Some other sections showed calcification in the cotyledons and a few areas with peculiar leucocytic infiltration of partly disintegrating villi. In some areas the picture was almost phlegmonous, the near-by villi showed different degrees of necrobiosis. The umbilical cord was not remarkable.

The strains isolated from blood, stool, and urine of the patient and from the placenta were identical. The organism was a motile, gram-negative bacillus which grew well on artificial media. It produced acid and gas from glucose, maltose, mannitol, dulcitol, xylose, rhamnose, and sorbitol, but not from lactose, sucrose, and salicin. Indole was not formed. The strain was studied further by Dr. Erich Seligmann, New York Salmonella Center, who identified it as *S. choleraesuis*.

When gram-negative bacilli were first recovered from the blood of the patient, an attempt was made to identify the strain by serologic methods. To this end, the supernatant fluid of the broth culture was

mixed with diagnostic horse sera. Polyvalent antimeningococcus serum caused strong precipitation, whereas anti-*H. influenzae* serum and normal horse serum did not. Antimeningococcus serum reacted in dilutions up to 1:100. Since it is well known that horse sera are more apt to give nonspecific reactions, precipitation tests were also set up with rabbit sera. Antimeningococcus types 1 and 4 sera produced a strong reaction with the supernatant of the culture. Whether this reaction is due to normal antibodies in these sera, or due to common antigenic components in *S. choleraesuis* and meningococci cannot be stated with certainty. The observation, however, clearly shows that the results of serologic methods used in the identification of microorganisms should always be considered together with morphological, cultural, and biochemical data, if erroneous conclusions are to be avoided.

Discussion

The exact incidence of Salmonella infections in the United States, particularly with respect to the distribution of the various types, remains undetermined. In part, this is due to the fact that many cases are not suspected clinically and others are not proved bacteriologically or serologically. Salmonella infections are not reportable in all states, while in others, as for instance in the State of New York, only cases of clinical paratyphoid fever, namely those caused by paratyphoid A and paratyphoid B (*Schottmueller*) bacilli, are reportable. It is important to emphasize that various members of the genus Salmonella cause a variety of clinical syndromes, among others, paratyphoid fever, gastroenteritis, bacteremia and septicemia, endocarditis, meningitis, and other purulent infections.

A search through the available literature failed to reveal any reports on Salmonella infections during pregnancy. On the other hand, paratyphoid bacilli have been encountered in septic abortion and puerperal sepsis as, for instance, in cases due to *S. choleraesuis* reported by Bornstein, Saphra, and Strauss² and by Roth.³ Noteworthy also is the fact that *S. choleraesuis* has been recovered as causative agent of salpingitis and parametritis (*Seligmann, Saphra, and Wassermann*⁴). Our case of *S. choleraesuis* bacteremia in pregnancy presents several interesting features. It should be emphasized that the correct diagnosis was made only by means of a routine blood culture. The strain was identified by the New York Salmonella Center. It seems reasonable to suggest that laboratories not equipped for the determination of the many types comprising the genus Salmonella should send subcultures to Salmonella Centers, such as the New York Salmonella Center under the direction of Dr. Erich Seligmann, or the Salmonella Center at Lexington, Kentucky under Dr. P. R. Edwards.

The fact that the patient developed specific antibodies in high titer during the course of the illness is additional proof of the pathogenic significance of *S. choleraesuis*. The agglutinin titer rose from less than 1:10 to 1:2,560.

Twelve days after the onset of the fever, stool and urine of the patient became positive for paratyphoid bacillus. It is not difficult to visualize the possible consequences that may result from the presence in a maternity hospital of a patient excreting *S. choleraesuis*, particularly, when one takes into consideration the fact that newborns and infants appear to be quite susceptible to Salmonella infections. For this reason, the patient was transferred to the department of contagious diseases as soon as the bacteriologic diagnosis of Salmonella infection was established.

The question arose as to whether or not intrauterine transmission of the paratyphoid bacilli had occurred. It is well known that typhoid bacilli may pass through the placenta. Diddle and Stephens⁵ recently reported a case of typhoid fever in a newborn infant whose mother was convalescent from the disease. These authors collected reports of 78 cases of typhoid fever during pregnancy from the literature. In 18 cases the data were incomplete and the diagnosis may well have been erroneous. In the remaining 60 acceptable cases, 31 developed the disease during the last trimester of pregnancy and were delivered of living infants. However, only 17 of these babies survived longer than 4 days.

In the case here reported, *S. choleraesuis* was present in the blood of the mother and in the placenta. The evidence at hand indicates that this organism did not invade the blood stream of the fetus. It may be assumed, therefore, that the death of the fetus was not due to infection per se. On the other hand, it is possible, although by no means certain, that the bacteremia of the mother was a contributing factor to the fatal outcome; in all likelihood, it was not the result of the toxemia.

Summary and Conclusions

A case of *S. choleraesuis* bacteremia during pregnancy is presented, apparently the first to be reported in detail in the American literature in recent years. The febrile illness began in the seventh month of pregnancy, 12 days prior to delivery of a macerated fetus. The patient excreted paratyphoid bacilli in feces and urine 11 days after the onset of the infection. On the twelfth day of the illness, specific agglutinins appeared in high titer. The placenta contained paratyphoid bacilli, but cultures of the blood and mouth of the fetus remained sterile. The patient recovered from the paratyphoid bacillus infection. Various aspects of Salmonella infections are discussed.

The authors wish to express their sincere appreciation for the identification of the strain to Dr. Erich Seligmann, New York Salmonella Center, and to Dr. Kornel L. Terplan for the histologic report on the placenta.

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THE CONTROL OF MENORRHAGIA BY PROLACTIN*

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OF ALL the dysfunctions that are associated with the menstrual cycle of women and which are of discomfort and even hazardous to the health of the patient, menorrhagia presents the most formidable problem to the clinician. Inasmuch as the physiology of uterine bleeding is not entirely understood, it is quite apparent that the physiological concept of malfunction of the menstrual cycle is likewise confused and misinterpreted. In addition, failure to reproduce the phenomena of excessive uterine bleeding in the common laboratory animal has prevented adequate experimental investigation of this problem, and has led to empirical therapeutic procedures or radical surgical cures. Although many different forms of therapy have been suggested, none has assumed the position of a panacea for the control of excessive uterine bleeding. In view of the multitude of methods proposed for the alleviation of functional and pathological uterine bleeding, it is apparent that not one has been uniformly accepted as the ideal mode of therapy.

In a search for a satisfactory therapeutic tool to dam successfully the menorrhagic flow, we decided to investigate the possibilities of the lactogenic hormone, prolactin, since it was shown by Greenblatt et al¹⁻⁴ that blood from lactating women was a useful, though inconvenient mode of therapy in metropathic menorrhagia. Their rationale for employing this mode of therapy was based upon two lines of thought:

1. The only true period of physiologic amenorrhea other than pregnancy occurs during the interval of lactation.
2. Experimental evidence at that time had demonstrated the anti-gonadal effect of lactogenic preparations.

In view of the successful results obtained by adhering to such a therapeutic regimen and the recent demonstration of the luteotrophin action of lactogenic preparations, impetus was attained to investigate further the problem of menorrhagia, employing commercial preparations of lactogenic hormone as the therapeutic measure. The effectiveness of the blood of lactating women in suppressing excessive uterine bleeding, as described in earlier reports, might well be ascribed to the presence of lactogenic hormone in the blood stream at this time.⁵⁻⁶

While this work was in progress, Hall⁷ reported on the efficacy of lactogenic preparations in controlling excessive uterine bleeding. In presenting the results of this investigation, we substantiate the findings

*This study was supported in part by a grant from Armour Laboratories, Chicago, Ill., to the Department of Experimental Medicine administered by Robert B. Greenblatt.

of earlier work¹⁻⁴ and those of Hall and also present some preliminary data on the effect of prolactin upon the normal menstrual cycle and threatened abortion.

Procedure

Two types of purified prolactin preparations were employed in this investigation.* One type of preparation was available as a sterile powder and supplied with a solvent (saline or distilled water) to be added before using, while the other preparation was made up in solution form. We have found the powdered preparations to be more effective in treatment and saline to be the preferred solvent. The lactogenic hormone was administered for various periods of time to 43 women exhibiting organic or functional uterine bleeding. In patients suffering from organic disturbances such as fibromyoma, pelvic inflammatory disease, etc., it is to be emphasized that the lactogenic medication was purely palliative in action and was not employed with the intention of alleviating the organic disturbance. By controlling the excessive uterine bleeding in these patients, a suitable interval was provided between the cessation of bleeding and preparation of the patient for a more final and complete cure.

The doses of prolactin that were employed ranged from 100 to 250 International Units per injection and were administered subcutaneously every day, or second day during the abnormal period of bleeding. In several cases where the menorrhagia had been of long duration, it was necessary to administer 100 to 200 I.U. of prolactin in daily doses for 4 to 8 days before the bleeding could be checked. When possible, suction curettages were undertaken to determine the condition of the endometrium before and during administration of prolactin. Uterine biopsies were taken for a twofold purpose:

1. To determine the type of endometrium from which bleeding occurred.
2. To ascertain activity of the ovary by noting its physiologic effect upon the endometrium.

Operative specimens of the uterus or ovaries, or both, were also obtained and studied, particularly in patients undergoing hysterectomy, for additional evidence on the physiologic action of prolactin.

In addition to the patients exhibiting abnormal bleeding, three women with normal cycles were treated with daily doses of prolactin to determine the effect of the lactogenic hormone upon the length of cycle and endometrial histology.

Preliminary data are also presented on the effect of prolactin in six cases of threatened abortion. Four patients gave a history of previous abortion, while two presented a history of earlier uncomplicated pregnancies. These patients were all subjected to an intensive course of prolactin therapy in an attempt to control the untoward symptoms which were associated with cramps and bleeding.

Results

The data summarizing the results obtained with prolactin are presented in Table I, where the clinical outcome is classified as follows:

- (a) Excellent—indicating prompt and complete control of the uterine bleeding.

*Prolactin preparations were generously supplied by Armour Laboratories, E. R. Squibb and Sons, and Winthrop Chemical Co.

- (b) Good—referring to those cases where longer therapy was necessary to control bleeding.
- (c) Fair—those cases in which bleeding was largely suppressed, but never completely inhibited, so that the patient exhibited a prolonged but mild menstrual flow during the administration of prolactin.
- (d) Poor—indicating no diminution of bleeding following lactogenic treatment.

TABLE I. CLINICAL EFFECTS OF PROLACTIN

| CHIEF COMPLAINT | ASSOCIATED WITH | CLINICAL RESULTS | | (NUMBER OF CASES) | |
|---------------------|-------------------------------------|------------------|------|-------------------|------|
| | | EXCELLENT | GOOD | FAIR | POOR |
| Menorrhagia | Functional bleeding | 8 | 7 | 1 | 1 |
| Menorrhagia | Uterine fibromyoma | 8 | 12 | 1 | 2 |
| Menorrhagia | Cystic ovaries | 3 | 3 | 2 | 1 |
| Menorrhagia | Chronic pelvic inflammatory disease | 5 | 4 | 3 | 2 |
| Dysmenorrhea | Menorrhagia | 5 | 3 | 4 | 2 |
| Threatened abortion | Cramps and bleeding | 3 | 0 | 0 | 3 |

In the accompanying chart, menorrhagia is listed as being associated with other clinical symptoms or entities such as fibromyoma of the uterus, cystic ovaries, chronic pelvic inflammatory disease, etc. In presenting the summary in a chart form, some cases have been itemized in more than one group due to dual complaints. For example, a patient with fibromyoma might also be subject to dysmenorrhea at onset of the menses which, in turn, might be menorrhagic in nature. Likewise, cystic ovaries or fibromyoma might be present in a menorrhagic patient. The clinical results are evaluated on the basis of the chief complaint and not upon the improvement of the associated conditions. Hence, although 43 patients in all were treated for abnormal bleeding, a great many more notations are included in the chart due to concomitant symptoms.

From Table I it is apparent that lactogenic hormone is of proved value in controlling excessive uterine bleeding. It was equally effective in controlling menorrhagia, whether functional or organic in origin.

Of the 17 women suffering from functional menorrhagia, i.e., menorrhagia associated with no pathologic manifestations, two failed to respond favorably to the hormone therapy. All the patients in this group gave a history of excessive bleeding for at least one cycle prior to their appearance in the clinic. In fact, a majority of the patients offered the information that the excessive menstrual periods were of long duration and the interval between the menstrual flow was obvious only by its brevity. Uterine biopsies taken in this group of patients on the first day of menses exhibited predominately an estrogenic or cystic glandular hyperplastic endometrium, although several cases were observed where menorrhagia was associated with a secretory endometrium. Daily injections of 100 I.U. of prolactin were administered during the period of uterine bleeding. The clinical success of this mode of therapy was indicated by the cessation of bleeding that occurred in all but two of the 17 patients treated. The severity of bleeding in subsequent cycles depended upon the regimen that was employed. In those cases where prolactin was injected on the first day of subsequent menses and continued for 2 to 3 days, bleeding was well controlled. Of those patients

who did not receive further treatment after one successful therapeutic course with prolactin, five had normal cycles and two reverted to their original condition of excessive and prolonged uterine bleeding.

Menorrhagia associated with fibromyoma of the uterus responded very satisfactorily to prolactin therapy. These patients were more resistant to treatment than those with functional menorrhagia and required daily doses of 100 to 200 I.U. of prolactin for a period of 4 to 8 days, whereas patients with functional menorrhagia required only 100 I.U. per day for 3 to 6 days. All the patients in this group had been suffering with menorrhagia for at least three months and one third of these patients bled almost continually. The clinical results with prolactin were pronounced, although not as favorable as in the patients with functional menorrhagia. Three patients failed to respond satisfactorily to prolactin therapy. As has been mentioned before, prolactin was not administered to these patients for the purpose of causing a regression of the uterine fibromyomas, but was employed so that the patient might be placed in proper physical condition to withstand the necessary surgery. This procedure was resorted to since clinically, many of these patients exhibited a severe secondary anemia as a result of their bouts of excessive uterine bleeding. In no instance in cases of fibromyomas of the uterus does the use of prolactin imply a substitute for surgery.

Menorrhagia noted in the presence of cystic follicles in the ovaries likewise required persistent prolactin therapy to control the excessive uterine bleeding. The presence of cystic ovaries was determined by palpation and then confirmed by laparotomy, or was ascertained by surgery alone. In those cases in which prolactin was effective, it was necessary to use daily doses of 100 to 200 I.U. of prolactin for periods of 5 to 8 days before bleeding could be controlled. Inasmuch as all the patients in this group were subject to pelvic surgery, data on the menstrual periods following therapy is meager. However, it may be said that three patients who had been successfully treated with one or two courses of prolactin had 2 to 4 normal menstrual periods prior to the time of their operations.

Menorrhagia when seen with concomitant chronic pelvic inflammatory disease, was aided by prolactin therapy, although we had our greatest percentage of failures in this group of patients. Two patients did not respond to prolactin, and in three, prolactin induced a diminution of bleeding but not complete arrest. However, of the nine patients that responded to prolactin therapy, all but one resumed normal menstrual periods after two or three courses of treatment. This ability of prolactin to exercise curative effects after cessation of therapy is of importance and implies a degree of permanency in the corrective effect of prolactin upon excessive uterine bleeding in certain selected cases.

Fourteen patients, although complaining of menorrhagia, also experienced severe dysmenorrhea either during the entire menorrhagic period, or on the first few days of the menstrual flow. Of these women, eight obtained relief from their painful menstruation accompanied by cessation of the abnormal bleeding. Three of the six patients not obtaining relief from dysmenorrhea with prolactin, did receive prompt relief from their menorrhagic syndrome.

In the treatment of threatened or habitual abortion, the results observed with prolactin were at times promising and at times disappointing. Six cases in all were treated. All the patients gave a history of previous pregnancies which in four patients were associated with missed or habitual abortion. In three patients, all having previous abortive

interruptions of pregnancy, the results were spectacular. When first seen, these patients had severe abdominal cramps accompanied by profuse uterine bleeding. After daily doses of 400 I.U. of prolactin (200 I.U. administered twice per day) for 3 to 4 consecutive days, abdominal cramps became quiescent and bleeding ceased. One patient with a history of two previous abortions experienced an attack similar to those which had precipitated the other abortions, but this time she received a course of prolactin therapy. All threatening symptoms subsided after this one series of injections, and she delivered a normal infant at term several months later. In the other two cases of threatened abortion that were successfully controlled by prolactin, it was necessary to administer prolactin during 4 to 6 successive attacks of severe abdominal cramps and bleeding. Immediately after an intensive but brief course of prolactin treatment, the muscular contractions subsided and bleeding was suppressed. In these latter two cases, one viable infant was delivered at term to a woman who had not been able to carry her pregnancy to term in three previous instances. Prolactin had been administered to this patient at each one of several seizures of threatened abortion and had adequately controlled her adverse symptoms. The other patient who had responded favorably to prolactin when subjected to threatening seizures finally delivered a viable 7-month fetus following a short period of severe uterine contractions and bleeding. This premature delivery could not be prevented since the patient failed to inform us of her condition early enough so that effective prolactin treatment could be instigated. Prior to this, the patient had had four seizures of cramps and bleeding which had been completely controlled by prolactin. The three cases that did not respond to prolactin therapy aborted during treatment. It is conceivable that in these cases some untoward factor was involved and/or the prolactin injections were started before their maximal influence could take effect and their further action was interrupted by the spontaneous abortion.

Prolactin when administered to normal cyclic women in doses of 300 to 500 I.U. per week for periods of 7 to 10 weeks, did not have any appreciable effect upon the length of the cycle, amount of bleeding or condition of the endometrium. Uterine biopsies taken at various intervals during the period of lactogenic therapy microscopically did not show any deviation from the normal. Two of the women who had been menstruating regularly from a progestational endometrium continued to do so during the administration of the lactogenic hormone. In addition, it might be said that the regularity of these cycles was not disturbed, and there was no evidence of an atrophic endometrium resulting from the continued prolactin medication. The third patient, exhibiting regular cycles, but whose endometrial studies indicated that she was subject to anovulatory cycles, continued to menstruate regularly without alteration of the usual endometrial morphology. In this patient, uterine biopsies, taken prior to treatment with lactogenic hormone on the first day of menses, revealed a proliferative or estrogenic endometrium. This was not altered in subsequent menstrual bleeding during which repeated injections of prolactin had been administered over a period of seven weeks. In addition to these data, observations made in the group of menorrhagic patients also indicated that prolactin exerted little if any effect upon the morphology of the endometrium. Uterine biopsies taken from many of the menorrhagic patients before commencement of prolactin therapy showed predominately an estrogenic, or proliferative type of endometrium. The prolactin therapy which

successfully controlled the excessive uterine bleeding did not bring about any change in the morphologic appearance of the menstrual endometrium, regardless of its histologic make-up before treatment.

Discussion

The control of uterine bleeding by lactogenic hormone raises the question of its possible mode of action. Evidence from animal experiments of earlier investigators and also endometrial studies in the human have indicated that prolactin might conceivably have an antigonadal action. This has been demonstrated by the action of prolactin in decreasing gonadal size in fowls⁸ and suppressing estrous cycles in rats.⁹⁻¹² In the human, endometrial studies¹³⁻¹⁵ have shown that only a relatively small number of women ovulate during the period of lactation. In addition, those women not ovulating, while exhibiting a proliferative endometrium, show one of an early differentiating type, or one associated with low ovarian activity.

In contradistinction to the supposed ovarian negating action of prolactin, recent experimental evidence has shown that the suppressing effect of prolactin upon the estrous cycle of the rat may be ascribed, not to the inhibitory effect of prolactin upon the ovary, but actually to its ability to prolong and maintain the function of the corpus luteum. Administration of lactogenic preparations to adult female rats results in cessation of estrous cycles with the persistence of one crop of active corpora lutea.¹⁰ Evans, et al.,¹⁶ showed that the corpora lutea persisting during lactogenic administration are physiologically active and will induce deciduomata formation in hypophysectomized adult rats. It remained for Astwood¹⁷ to postulate and demonstrate the presence of a third gonadotropic hormone, luteotrophin, which regulates the activity and maintains the function of formed corpora lutea. Since purified lactogenic preparations are capable of maintaining active corpora lutea in the rat, the lactogenic hormone has become allied with the luteotrophic hormone of Astwood.

In considering which one of these properties, ovarian negating or luteotrophic action attributed to prolactin, is the *modus operandi* in controlling uterine bleeding, it is difficult to reconcile our results with the ovarian negating action of prolactin. In our study of women with normal cycles and those suffering with menorrhagia, massive doses of prolactin did not in any way alter the cyclic manifestations, or cause retrogressive changes to take place in the endometrium. There was no evidence of gonadal inhibition as determined by repeated examinations of the uterine scrapings and operative specimens of the ovaries. On the other hand, it is conceivable that the lactogenic preparations are effective in controlling abnormal uterine bleeding through their luteotrophic properties. It is possible that the administration of these pituitary extracts enhances the production of the corpus luteum hormone or hormones, and provide thereby a proper hormonal balance for the

control of menorrhagia. This seems to be the most logical explanation of the satisfactory results in which not only menorrhagia was controlled, but threatened abortion was held in abeyance.

Summary

1. Menorrhagia, either functional or organic in nature, was favorably influenced by administration of lactogenic preparations extracted from the pituitary gland. Menorrhagia associated with uterine fibromyomas, cystic ovaries, or chronic pelvic inflammatory disease was suppressed in the majority of patients by administration of prolactin. Those patients, however, in the latter two categories were more resistant to therapy. Normal cyclic bleeding followed cessation of prolactin therapy in many of the patients receiving one or more courses of treatment. This permanency or semipermanency in the effect of prolactin afforded a sufficient interval to enable the patient to undergo a more strenuous regime to correct the underlying cause of the excessive uterine bleeding.

2. Some success was obtained in mitigating dysmenorrhea by prolactin therapy when it was associated with excessive uterine bleeding.

3. In addition, the signs and symptoms of threatened abortion were alleviated by administering prolactin to 3 of 6 patients giving a history of previous abortive interruptions of pregnancy.

4. Administration of lactogenic preparations to normal cyclic women did not have an appreciable effect upon the length of cycle, menstrual bleeding or morphologic appearance of the endometrium.

5. It is suggested that the effectiveness of lactogenic hormone in controlling uterine bleeding is probably linked with its luteotrophic properties.

6. In view of the innocuous effect of prolactin upon the normal menstrual cycle and corrective action in metropathic menorrhagia, we find its use is warranted in the control of excessive uterine bleeding.

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CESAREAN SECTION UNDER CONTINUOUS CAUDAL ANALGESIA

A Supplementary Report

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IN A preliminary report¹ the use of continuous caudal analgesia in 50 cases of cesarean section was reviewed. We have added 62 cesarean sections to our series and herewith present a report of our observations of the total of 112 cases. Seventy-three of the patients were operated upon at the Philadelphia Lying-in Hospital, 7 at the Jefferson Medical College Hospital, and 6 at the Philadelphia General Hospital. An additional 22 cases were managed by Dr. Edwards and Dr. Hingson at the Marine Hospital, Staten Island, and 4 cases are from Dr. John C. Hirst's service at the Preston Retreat, Philadelphia.

TABLE I. INDICATIONS FOR OPERATION

| | |
|--|----|
| Disproportion, twin pregnancy, toxemia | 1 |
| Disproportion, pre-eclamptic toxemia | 1 |
| Disproportion, previous section | 11 |
| Disproportion, pulmonary tuberculosis | 1 |
| Disproportion (cephalopelvic) | 62 |
| Diabetes | 2 |
| Eclampsia | 1 |
| Pre-eclampsia | 5 |
| Multiple uterine fibroids | 4 |
| Previous hysterotomy | 2 |
| Rheumatic heart disease | 3 |
| Heart disease | 8 |
| Previous difficult delivery | 3 |
| Uterine inertia | 1 |
| Epilepsy | 2 |
| Severe contractile burn scar of perineum | 1 |
| Advanced pulmonary tuberculosis | 3 |
| Premature separation of placenta | 1 |

The usual indications for cesarean section are listed in this table. We had only one opportunity to give continuous caudal analgesia when cesarean section was performed because of premature separation of the placenta, and the result was entirely satisfactory. We were particularly impressed with the prompt contraction of the uterus following removal of the child and the partially separated placenta. It has been our experience that good uterine tone does not exist when cesarean section for premature separation is performed under general anesthesia.

The following contraindications to the use of continuous caudal analgesia in cesarean section are essentially the same as in vaginal delivery:

1. Gross deformities of the spine, particularly of the sacrum (occur less than once in 200 cases).

2. Tumors of the spinal canal, including pilonidal cysts.
3. Local infections around the sacral hiatus.
4. History of sensitivity to one of the cocaine derivatives or their substitutes.
5. Profound anemia, unless supplemented with transfusion and oxygen inhalation.
6. Placenta previa. We have consistently hesitated to use this technique in placenta previa because of possible hemorrhage associated with relaxation of the cervix. It should never be used if the patient is in labor, but we believe it would not be contraindicated if the patient is not in labor and the cervix is fairly thick. We have not had the opportunity of using it in such a case.
7. Hysterical patients, or those physically unsuited. Patients with vasomotor instability or of low mentality, because of a fear of being conscious during the operation, are poor subjects and do not cooperate well.
8. Extremely obese persons in whom the sacral hiatus cannot be palpated.
9. A low lying dura is an absolute contraindication. If the needle should enter the dura and spinal fluid is aspirated, the method should be discontinued as this would result in a total spinal anesthesia.
10. Patients who have a glandular imbalance. In our series both of the patients who had a severe drop in blood pressure showed signs of glandular disturbance.

Preoperative Preparation of the Patient

We believe preoperative preparation is particularly important when a patient is to remain conscious during a surgical procedure. Several points must be considered.

1. Mental reassurance is necessary. Because of the wide publicity given to this new method, facts are often distorted, and as a result some patients fear "a spinal." A careful explanation of the method and procedure before operation usually allays any fear and in every instance postoperatively the patient is enthusiastic about the results. The husband should be informed that at least a half hour must elapse before the operation can be started so that he will not expect her to return to her bed in the usual short period of time. Many patients who had a previous cesarean section under gas-ether anesthesia remarked how much smoother their convalescence was following continuous caudal analgesia.
2. The patient is given $1\frac{1}{2}$ grains (0.1 Gm.) of a barbiturate the previous night and again one hour before operation. This brings her to the operating room in a quiet and cooperative mood for the administration of the drug.
3. Adequate fluid intake preceding operation is important. All cesarean section cases should have blood typing and cross-matching done previously and it is advisable to have plasma available.
4. Soapsuds enema and catheterization with an indwelling catheter is an important part of preoperative preparation.
5. Absolute quiet must be maintained in the operating room and the patient should be reassured by the anesthetist throughout the procedure.

Technique

The following is the technique of administering continuous caudal in cesarean section, which varies somewhat from that followed in vaginal delivery.

1. One and five-tenths per cent metycaine in isotonic solution of sodium chloride or isotonic solution of three chlorides (Ringer's solution) is prepared.

2. The continuous caudal needle is inserted and the apparatus adjusted as for obstetric analgesia.

3. An initial test dose of 8 c.c. is administered with careful check by aspiration to ascertain whether or not the needle is within the subarachnoid space or a blood vessel. In this injection of 8 c.c. we are now adding 50 mg. of ephedrine hydrochloride, except where a hypertension is present, to preclude any drop in blood pressure. The hydrochloride solution is miscible with the Ringer's solution, whereas the sulfate is not as readily absorbed and is more likely to give side reactions.

4. A supplementary dose of 40 to 60 c.c., depending on the size of the patient, is administered. The patient is then placed on her back in a 5° Trendelenburg position and the level of analgesia is tested in twenty minutes.

5. If the level of analgesia has not risen above the umbilicus on both sides, a third dose of 20 to 40 c.c., according to the need of the patient, is administered.

6. When the level of analgesia on both sides is complete to the height of the eighth dorsal segment, the operation may be started. This level is usually attained about thirty minutes after the first injection. In debilitated patients, seriously ill with tuberculosis or heart disease, the procedure should be instituted forty-five minutes to one hour before operation and the level of analgesia developed more slowly.

7. In cesarean section patients we have been giving oxygen routinely for approximately ten minutes prior to delivery of the child. This has been found especially valuable in cases of threatened abruptio placentae, toxemia, and cardiac disease. We have observed that if the blood pressure drops and there is any deviation from normal in the fetal heart sounds, they will return to normal within one or two minutes following elevation of the patient's legs, the giving of a supplemental dose of ephedrine, and inhalation of oxygen.

The time required before absence of sensibility to pain is attained varies. The operation should never be started before the level of analgesia is correct and the time required for this should not be hastened by unnecessary and repeated injections of metycaine. In our series the minimum time required before starting the operation was ten minutes; the maximum time, one hour and twenty minutes; and the average time, thirty-four minutes.

The patient who required one hour and twenty minutes before the drug had reached the desired level, had been in the hospital eight weeks with severe cardiac disease. At the time of operation she was very orthopneic and could not be placed flat on the operating table nor in the desired 5° Trendelenburg position. Consequently, a much longer than average time elapsed before the analgesia reached the desired level.

Postoperative Care

At the conclusion of the operation the patient is given $\frac{1}{4}$ grain of morphine sulfate hypodermically. This eases the incisional pain as the analgesic effect subsides.

Recently, we have been allowing the patient a soft or full house diet the same noon or evening of operation. This regime has decreased our postoperative distention to a minimum. Most patients have had no gas pains and their convalescence has been accelerated.

Complications Associated With Continuous Caudal Analgesia in Cesarean Sections

1. Drop in blood pressure. The average drop in systolic pressure was 22 mm. which is less than the 26 mm. previously reported. Two patients had a severe drop in blood pressure which may have been due to sensitivity to the drug unrecognized prior to operation or to a glandular imbalance, of which both patients showed positive signs. We believe the improvement may be attributed to the use of 50 mg. of ephedrine hydrochloride given with the initial injection of 8 c.c. of meteyaine. The more recent cases showed less drop in blood pressure, their average being 14 to 16 mm. of mercury. We have found that the fall in blood pressure is in direct proportion to the height of ascent of the nerve block in the peridural space and to the pharmacologic efficiency of the drug. In those instances in which there is a rather sudden drop in systolic pressure, the elevation of the feet and legs to a right-angle position in relation to the trunk, thereby producing an auto-transfusion from the greatly dilated venous system of the extremities, will dramatically raise the blood pressure 20 to 40 points within less than three minutes. The legs can then be returned to their usual position slowly. The blood pressure can be maintained by a 5° Trendelenburg position of the patient. However, in refractory cases of hypotension, the use of 25 and 50 mg. ($\frac{3}{8}$ and $\frac{3}{4}$ gr.) of ephedrine hydrochloride intravenously will raise and maintain the blood pressure at a safe level. This initial fall in blood pressure is the most serious complication associated with the technique. It should be diligently watched for, since it occurs in about 25 per cent of cases from 12 to 30 minutes after the initial injection. The majority of these blood pressure drops have occurred just as the patient was being turned from the lateral Sims' position to her back. None of our cases showed any postoperative blood pressure abnormality.

A very interesting observation in every instance of cesarean section as well as in vaginal delivery, is the immediate rise in the systolic blood pressure, within seconds following removal of the child from the uterus. This return to the normal preoperative level varies from 10 to 60 mm. of mercury and may be attributed to the decrease in the vascular bed with the closure of the arteriovenous vessels of the uterus.

2. We have used the malleable needle in all cases but two. In the two cases the ureteral catheter technique was followed. We have had no instance of needle breakage. As the malleable needle becomes more disfigured and bent during cesarean section than during the usual vaginal delivery, it was never used more than once or twice for this procedure and was then discarded.

3. Morbidity. There were three cases who had a febrile postoperative course. One morbidity was due to a mild endometritis following a ten-hour labor with ruptured membranes before operation. The other 2 cases had postoperative pyelitis which cleared up after routine treatment was instituted.

4. Bladder dysfunction. In no instance was catheterization necessary beyond what is usually required following cesarean section. There was no post-partum bladder paralysis.

5. Infection at the site of the needle insertion or in the peridural space was not present in our series. After the initial dosage of 8 c.c. of metycaine the skin area about the needle is covered with a 5 per cent sulfathiazole or merthiolate ointment before the patient is turned on her back. We believe this technique minimizes the hazard of infection entering the site where the needle punctures the skin.

6. Blood loss. The average estimated blood loss in all of our cases was 100 c.c. This was a definite decrease over cesarean sections previously performed under general anesthesia. An ergot and posterior pituitary preparation is employed intramuscularly following extraction of the child.

7. Other complications, such as headache, backache, or nausea and vomiting, were minimal. Vomiting occurred in 10 per cent of the patients during the administration of the drug. Whether this was due to anxiety or to the action of the drug on the maternal organism is not known. Several headaches occurred in patients in whom the solution was injected rapidly, in an attempt to gain a higher level of analgesia. However, they were all transient in duration and soon disappeared.

There were no maternal deaths in our series. One fetal death occurred which we do not believe can be attributed to the analgesic agent. This baby was delivered of a seriously toxic mother at 5½ months' gestation and succumbed within eight hours after birth.

Comment

In 108 cases, perfect analgesia was obtained. Three failures were attributed to inability to insert the needle, and 1 was due to malformation of the sacrum.

TABLE II. TYPES OF OPERATION

| | |
|---------------------------------|----|
| Low classical and sterilization | 21 |
| Low classical | 54 |
| Low segment operation | 27 |
| Low classical, myomectomy | 3 |
| Low classical, salpingectomy | 1 |
| Waters modification of Latsko | 6 |

The type of operation depended upon the individual patient and whether she was in labor or whether an elective section was to be performed. The operating time varied from fifteen to seventy-five minutes, with the average length of time thirty-eight minutes. The safety of continuing repeated injections as long as required, thus obviating the necessity to hasten the operation, is the outstanding feature of this method of analgesia.

Metycaine was used in all of the cases. The minimum amount necessary was 25 c.c., the maximum 370 c.c., with an average of 76 c.c.

We feel that this is one of the best methods that we have tried and is perfectly safe when administered by a trained person in a well-equipped maternity department. Our decision is influenced by the improved convalescence of the mother with absence of postoperative discomfort, the immediate cry of the baby at birth, and the fact that no baby in our series required resuscitation.

As we have continued our study, we have become more impressed with the following features of this method: First, the drop in blood pressure has been materially reduced by the use of ephedrine hydrochloride in the initial dose of metycaine; second, the injection of the drug should be slow, and ample time given to allow perfect analgesia before the operation is started; third, the level of analgesia is maintained easily regardless of the length of operation; fourth, the use of this method is especially advantageous in cardiac cases, toxemias, and respiratory infections; and fifth, the families of the patients are enthusiastic and appreciative of the rapid and smooth convalescence of mother and baby.

Summary

Cesarean section under continuous caudal analgesia was performed in 112 cases with perfect results in 108. There were 4 failures attributed to inability to introduce the analgesic agent into the sacral canal.

There were no maternal deaths, and no serious postoperative complications. There were 3 cases of morbidity, but these are not attributed to the use of the analgesia.

One baby death occurred in a 5½ months' gestation and the other 111 babies were discharged from the hospital in good condition.

Due to an improvement in technique, the blood pressure drop in our recent cases was less than previously reported.

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ACUTE PELVIC THROMBOPHLEBITIS TREATED WITH CONTINUOUS CAUDAL ANESTHESIA

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THE literature during the past year has been replete with reports of continuous caudal anesthesia in obstetrics, but there has been very little written on this procedure as a form of therapy in other conditions.

During the past six months at Providence Hospital, we have used this method in ten cases of acute pelvic thrombophlebitis, with very good results.

While we realize that this is a small series of cases, the results obtained warrant its further investigation by other observers.

The technique and contraindications are essentially the same as in obstetrics.

Following are two fairly typical case reports:

CASE 1.—Mrs. M. B., a 24-year-old primipara, had vaginal bleeding three weeks before her expected date of confinement and was delivered by classical cesarean section for ablatio placentae. Postoperatively, a lobar pneumonia developed which responded to sulfonamide therapy. She had a wound infection which was still draining when we first saw her, six weeks post partum. At this time, there was an acute pelvic thrombophlebitis of three days' duration. The whole left leg was swollen, blanched and extremely painful. Her temperature was 102° F., and the pain was unrelieved by ¼ gr. doses of morphine.

That evening a caudal anesthetic was started and continued for four hours. Following this the pain was permanently relieved, the extremity became warm, and the swelling began to subside.

The next day her temperature was 99.2° F., and there was slight ankle edema.

She left the hospital 48 hours following the caudal treatment, symptomatically cured.

CASE 2.—Mrs. H. J. S., developed an acute pelvic thrombophlebitis of the left leg three weeks postoperatively following a supravaginal hysterectomy.

She was readmitted to the hospital and a caudal anesthetic administered.

For 24 hours she had complete relief of pain, but the elevated temperature and swelling persisted.

Forty-eight hours after the original caudal injection, another was given, following which her symptoms and temperature completely subsided.

This was the only case in this series in which a second treatment was necessary.

We would first like to describe what we mean by acute pelvic thrombophlebitis. This is that type of intravenous clotting which is associated with inflammation of the vein wall (thrombophlebitis) and we will also only consider the most common clinical form, thrombophlebitis of the femoro-iliac vein, which gives us the typical picture of phlegmasia alba dolens. No attempt will be made to discuss the other types of intravenous thrombosis, which are equally important, such as partial or complete venous occlusion by an intravenous clot, unassociated with any inflammation of the vein wall (phlebothrombosis), or of thrombophlebitis of a superficial vein or of suppurative thrombophlebitis, all of which we believe require surgical treatment (ligation).

There is little difficulty in recognizing phlegmasia alba dolens; the patient is quite ill, has fever, a marked amount of pain in the affected limb and the extremity is swollen and white. Ordinarily, with elevation of the affected limb, rest and external heat, we would expect persistence of fever for several weeks and of edema for several months, with a long period of partial disability. However, with the use of sympathetic block by caudal anesthesia we have definitely reduced the time element in the alleviation of these symptoms to a matter of days.

A concept of the underlying etiological factors and pathology involved will give a better understanding of the rationale of this form of nerve block as a method of treatment for this condition. We will discuss the causes of phlegmasia alba dolens first in general, and then specifically.

In general, this is the most common form of thrombophlebitis because there is greater circulatory retardation in the lower extremities postoperatively or post partum, compared with the upper extremities. These patients will lie quietly in bed, seldom moving their lower extremities. Also Fowler's position causes circulatory retardation in the veins of the lower extremities, which is made worse by flexing the knees. Another factor in the movement of blood in the venous system is the negative pressure in the thorax. Postoperatively deep breathing is limited by the patient because it is painful, resulting in a decrease in the intrathoracic negative pressure and so favoring circulatory stasis. Increased abdominal tension also causes circulatory stasis in the lower extremities by direct pressure, due to too tight bandaging, or to gas or fluid within the intestine associated with ileus. The clot occurs more often in the left lower extremity than the right because the left common iliac vein is smaller than the right, it joins the inferior vena cava at a more acute angle than does the right, and it is crossed over by the iliac artery.

Specifically there are certain factors which predispose to the formation of a clot, the first is an inflamed vein wall and the next most important factor is tissue injury due to operative or accidental trauma, or by invasion of inflammation, or malignant disease. The toxic substances absorbed from this damaged tissue decreases the albumin content and increases the globulin content of the blood so that their ratio is dis-

turbed. This results in changes in the electrical charges of the formed blood, so that instead of normally repelling each other they become attracted to one another and so form a center for clot development. This explains why the platelets and erythrocytes and leucocytes show an increased agglutination tendency.

Pathology of Thrombophlebitis

It has been generally accepted that the edema in thrombophlebitis is due to increased venous pressure, produced by the blocking of the large vein draining the extremity by the clot. This is not true, because these patients can be relieved of their edema often within a week, long before the clot has disappeared. An understanding of the true pathology underlying "milk leg" will show how logical the use of sympathetic block is in these cases.

In thrombophlebitis there is set up in the thrombophlebitic segment impulses which are carried over the sympathetic nervous system producing spasm of the arterioles and venules. Normally, there is an interchange of intravascular and perivascular fluids. Fluid leaves the vascular tree at the arteriole extremity of the capillary because of filtration pressure. Fluid returns to the vascular system through the lymphatics and by absorption into the blood stream at the venule end of the capillary—this fluid exchange is normally in balance. However, when we have a spasm of the arteriole, the blood flow through the capillary is diminished and a relative anoxia occurs, this anoxia increases the permeability of the capillary endothelium and there is an abnormal exudation of fluid from the vascular system into the perivascular spaces. Once the fluid gets out, it has difficulty in getting back because the pump responsible for the movement of lymph, namely arteriolar pulsation, is no longer present so that fluid getting into the lymphatic system is not transported back to the blood vascular system. Also the increased pressure on the venule end of the capillary tends to prevent the normal absorption of fluid from this site.

Therefore, if we can prevent or break the vasoconstrictor impulses passing to the arterioles and venules from the sympathetic ganglion, the blood supply to the capillaries is re-established. The anoxia of the capillary wall is relieved by the return of normal oxygen tension and the previously increased permeability of the capillary is prevented. The excessive exudation of fluid outside the capillary is stopped. Also the arteriolar pulsation which is responsible for the movement of lymph is re-established so that the fluid can be removed from the extremity. By relieving the spasm on the venule, absorption of the perivascular fluid into the capillary is favored and this is the reason why patients with thrombophlebitis, in whom the thrombus is still present, have relief of their edema following lumbar sympathetic block. The clot has been firmly attached to the vein wall by the inflammatory process and there

is no danger of it breaking loose. With the return of the normal blood supply and vascular balance, the inflammation in the affected vein quickly subsides and the patient is clinically well.

Treatment of Phlegmasia Alba Dolens

Preventive or prophylactic treatment is of first importance. Patients should have their heart conditions corrected as well as possible before delivery or operation, since it is well known that the incidence of thrombosis is much higher in these cases if uncorrected, probably due to circulatory retardation. Correction of varicosities by either compression bandages, or by ligation and injection before delivery or operation is indicated. Foci of infection, obesity, blood dyscrasias (anemic and polycythemic patients have increased clotting tendencies) should all be treated beforehand. During the delivery or operation, we should try to be as atraumatic as possible, since it is the damaged tissue which releases the toxic substances which cause increased clotting tendency.

During the puerperium and postoperatively, normal water balance should be maintained. We should avoid postures favoring circulatory stasis of the lower extremities such as Fowler's position, especially when combined with flexion on the thighs on the trunk, and the knee on the thigh. The patient should actively contract the muscles of the lower extremities by forcefully flexing the feet against a resistance and the legs should be flexed repeatedly. We should also encourage respiratory stimulation by having the patient take ten to fifteen deep breaths every hour, thus the negative pressure in the thorax is increased and this favors the return flow of blood to the heart. Increased abdominal tension should be prevented by avoiding tight compression bandages on the abdomen and by preventing ileus. There is a great tendency after operation for the nurse to apply adhesive as snug as possible to the surgically relaxed abdomen. Ileus can be avoided by observing the period of functional inactivity of the bowel postoperatively, by restriction of what is taken by mouth during this period, the use of prostigmine and rectal tube, or, if necessary, the Wangenstein suction apparatus. Anticoagulants are of value but are not without danger, and should be used prophylactically only in patients with a history of previous intravenous thrombosis.

Thrombophlebitis of the femoro-iliac veins when it does occur either because the prophylactic measures were not used or in spite of them, can be best treated conservatively by caudal blocking of the sympathetics and early mobilization of the extremity. As soon as the swelling and fever have subsided, usually in a few days' time, they are allowed out of bed. They are instructed to wear compression bandages afterwards for a few weeks until the vascular balance is completely re-established.

Conclusions

We feel that by using the caudal method there are several advantages over the regional sympathetic block of the first, second, third, and fourth lumbar sympathetic ganglia.

Regional injection requires four punctures, caudal but one. We believe that the continuous bathing of the sympathetic chain for several hours is preferable to the one-injection technique necessitated by the regional block method.

In caudal nerve block we can tell when the needle is correctly placed by the classical signs, i.e., sciatic pain, progressive regional anesthesia, sphincter relaxation and finally by vasodilatation of the extremities. The same cannot be said of sympathetic nerve block because one cannot be sure if all the ganglia have been correctly injected.

In acute thrombophlebitis, we give 30 c.c. (low caudal) every hour until four doses have been given. With this intermittent method of injection, if there is any tendency for the vasoconstriction to re-establish itself after the effect of the drug wears off, we can immediately release the impulse by the next injection. Following the last injection, the needle is removed.

Finally, we feel that this is another form of therapy to be used in the treatment of acute pelvic thrombophlebitis and that it offers certain advantages over regional sympathetic block.

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VAGINAL ANTISEPSIS

A Comparative Study of Bimerphen Solution* in 910 Consecutive Deliveries

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THE purpose of the present study is to compare Bimerphen solution with other antiseptics which have been used for vaginal instillation prior to delivery.

There has been a great deal of controversy regarding the value and rationale of using predelivery antiseptic vaginal instillations, but the results from many studies¹⁻⁶ definitely establish the value of this procedure. Morbidity and mortality figures released from several centers prior to the use of vaginal instillation indicate that a figure between 15 and 20 per cent morbidity is to be expected. Following the adoption of this procedure, the figures show a marked reduction in morbidity and mortality.

During the third trimester of pregnancy, there is an increase in vaginal secretions which is accepted as a normal physiologic reaction. These secretions are usually alkaline in character and in most instances show a pH well above 6.0. At this pH or above, abnormal bacterial inhabitants and pathogenic organisms (aerobic and anaerobic) are provided with an environment conducive to their growth and propagation, thus presenting a potential source, at least, of post-partum infection.

Despite the arguments presented against the use of vaginal instillations,¹ the statistics from various clinics indicate that the procedure is of value, regardless of the antiseptic used.

In 1926, Schwarz and Brown² initiated the routine use of mercurochrome, iodine and glycerin, and in 1930, 1 per cent neutral acriflavine in glycerin. Morbidity figures were reduced by one-half.

Brown³ in 1940, reported 13 deaths in 9,529 deliveries prior to vaginal antiseptics, but after the advent of vaginal instillations, no deaths due to sepsis occurred in 12, 913 deliveries.

Mayes¹ reports that at the Brooklyn Methodist Hospital where the mercurochrome technique had been in use for five years, no deaths occurred from sepsis in 5,648 deliveries and the morbidity figure for the period was 2.3 per cent.

Tritsch⁴ in a comparative study using amphyl and 4 per cent aqueous mercurochrome reported equal efficiency in both preparations. The incidence of infection in spontaneous deliveries was 5.4 per cent and

*Bimerphen solution, supplied by the Medical Research Division, Sharp & Dohme, Glenolden, Pennsylvania, is a solution of hexyl m-cresol 1:1,000 and phenyl mercuric acetate 1:1,000 in an aqueous propylene glycol base.

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in operative deliveries 7.4 per cent; the incidence of infection in primiparas was 9.2 per cent (due to greater operative procedures) and 4.6 per cent in multiparas.

Ziegler and Austin⁵ reported a total of 5,140 deliveries and were able to show a decrease in morbidity figures after the use of tincture of merthiolate 1:2,500 solution as vaginal instillation. In 1932, prior to the use of the solution, the morbidity was 15.21 per cent, while in 1937, following the adoption of the procedure, the figure was 9.16 per cent (including 287 cases not receiving the instillations).

Mayes,⁶ reporting the use of 4 per cent aqueous mercurochrome solution in 13,763 deliveries at the Methodist Hospital, Brooklyn, shows a reduction of morbidity from 14.8 per cent to 5.3 per cent. Two deaths from sepsis occurred in 25,347 vaginal deliveries while none have occurred in the last 11,000 deliveries. They have also used 1:1,000 solution of zephiran on 837 cases with a morbidity rate of 8.7 per cent.

Here at Hahnemann Hospital a previous series of 1,000 patients was studied in which 'S. T. 37' hexylresorcinol solution was used. A morbidity figure of 7.0 per cent was obtained. Four per cent mercurochrome was also tried on 326 cases showing a morbidity figure of 6.94 per cent. Ten per cent mercurochrome, used as an external spray to the genitalia only, produced morbidity figures of 10.28 per cent in 523 patients. Our experience with the use of amphyl, with one routine vaginal examination allowed for each patient, showed morbidity figures of 12.02 per cent in 707 patients. No vaginal examinations were permitted when the other antiseptics were used.

Assuming that vaginal antisepsis is rational and a definite aid in the reduction of morbidity, we feel that the requirements for a suitable agent should meet the following:

1. Safety to mother and child.
2. Germicidal and bacteriostatic.
3. Rapid in action.
4. Easy to apply.
5. Does not stain linens, etc.
6. Readily available.
7. Economical.

Bimerphen solution is a combination of hexyl m-cresol 1:1,000 and phenyl mercuric acetate 1:1,000 in 75 per cent propylene glycol. The combination of the two compounds supplies marked bactericidal as well as great bacteriostatic activity. The solution is effective in the presence of serum or other body fluids. The pH of the solution is 3.6 which provides additional unfavorable environment for the growth of pathogenic bacteria. The germicidal activity of propylene glycol is well recognized. Bimerphen solution does not stain tissues or bed linens.

The technique of administration was as follows: one-half ounce Bimerphen solution was instilled into the vagina with a sterile Asepto

syringe. The original instillation was given on admission to the floor and repeated in four hours if the patient was undelivered, and repeated again in four hours if the patient was still undelivered.

These 910 consecutive cases were divided on the basis of number of doses of bimerphen received prior to delivery. Morbidity figures are based on two or more temperatures of 100.4 or more, occurring at any time in the puerperium excluding the first twenty-four hours after delivery.

Table I, a summary of pertinent data, reveals some rather interesting information. Although we were somewhat handicapped in carrying out this study due to the lack of help, rapid turnover in personnel, and loss of our obstetric resident for a period of time, we were gratified at the results obtained.

TABLE I. SUMMARY OF DATA COLLECTED ON PATIENTS TO WHOM 1-2-3 DOSES OF BIMERPHEN SOLUTION WERE ADMINISTERED

| NO. AND PERCENTAGE OF PATIENTS IN EACH GROUP | 3 DOSES | | 2 DOSES | | 1 DOSE | | TOTAL | |
|--|---------|------|---------|-------|--------|------|-------|-------|
| | NO. | % | NO. | % | NO. | % | NO. | % |
| | 297 | 32.6 | 215 | 23.6 | 398 | 43.7 | 910 | 100.0 |
| At term | 279 | 94.0 | 197 | 91.6 | 370 | 93.0 | 846 | 92.9 |
| Premature | 18 | 6.0 | 18 | 8.4 | 28 | 7.0 | 64 | 7.1 |
| Primiparas | 167 | 56.2 | 84 | 39.1 | 78 | 19.6 | 329 | 36.15 |
| Multiparas | 130 | 43.8 | 131 | 60.9 | 320 | 80.4 | 581 | 63.85 |
| Operative incidence | 16 | 5.3 | 2 | 0.9 | 2 | 0.5 | 20 | 2.19 |
| Perineal injuries (including episiotomy) | 178 | 59.9 | 113 | 52.5 | 149 | 37.4 | 440 | 48.3 |
| Morbidity (total) | 20 | 6.7 | 16 | 7.44 | 25 | 6.28 | 61 | 6.70 |
| Morbidity (pelvic) | 16 | 5.38 | 14 | 6.51 | 22 | 5.53 | 52 | 5.71 |
| CAUSES OF MORBIDITY | | | | | | | | |
| A. Endometritis | 12 | 60.0 | 8 | 50.0 | 16 | 64.0 | 36 | 59.0 |
| B. Parametritis | 1 | 5.0 | 2 | 12.5 | 3 | 12.0 | 6 | 9.8 |
| C. Infected perineum | 3 | 15.0 | 3 | 18.75 | 2 | 8.0 | 8 | 13.1 |
| D. Medical, etc. | 4 | 20.0 | 3* | 18.75 | 4* | 16.0 | 11 | 18.0 |

*Includes exacerbation of gonorrheal salpingitis—1 case.

The majority of the group receiving three instillations were primiparas (56.2 per cent). This fact was due to the longer labor usually making them available for three doses. Those receiving but one dose were delivered within the first four hours after admission; this group shows a heavy percentage (80.4 per cent) of multiparas.

The perineal injury group, which includes episiotomies, first, second, and third degree lacerations, revealed an interesting finding. The group receiving three doses of Bimerphen solution (32.6 per cent) showed a morbidity of 5.38 per cent while the group receiving but one dose (43.7 per cent) had a morbidity of 5.53 per cent. The operative incidence of the first group was 5.3 per cent while in group three, it was 0.5 per cent. These figures would seem to point to the effectiveness of Bimerphen when administered in at least three doses. In spite of the fact that the operative incidence was some ten times greater in the first group and the percentage of perineal injuries was significantly greater, the morbidity figures closely approximate each other—5.53

and 5.38 per cent. It is well established that the greater the operative incidence and perineal injuries, the higher the morbidity figures.

There were 440 cases of perineal injuries with a morbidity figure of 6.8 per cent. The group without perineal injury (470) showed a morbidity figure of 4.68 per cent. This comparison bears out our previous statement.

Morbidity causes included endometritis, parametritis and infected perineum. No significant difference in figures was evident in the three groups. Medical, breast, and renal causes were excluded in compiling these figures.

TABLE II. COMPARISON OF RESULTS WITH USE OF VARIOUS ANTISEPTICS

| | AMPHYL | 10% MERCURO- CHROME EXT. SPRAY | 4% MERCURO- CHROME | S. T. 37 SOLUTION | BIMERPHEN SOLUTION |
|---|--------|---|--------------------------|----------------------|-----------------------|
| Number of cases | 707 | 523 | 326 | 1000 | 910 |
| At term | 684 | 500 | 303 | 917 | 846 |
| Premature | 23 | 23 | 23 | 83 | 64 |
| Primiparas | 264 | 187 | 134 | 389 | 329 |
| Multiparas | 443 | 336 | 192 | 611 | 581 |
| Forceps | 14 | 8 | 11 | 30 | 17 |
| Versions | 4 | 2 | 1 | 2 | 3 |
| Perineal injuries (including episiotomy) | 256 | 198 | 144 | 499 | 440 |
| Morbidity (total percentage) | 20.50 | 22.30 | 13.50 | 12.0 | 6.70 |
| Morbidity (pelvic percentage) | 12.02 | 10.28 | 6.94 | 7.0 | 5.71 |

Table II is a summary of our findings on the use of the various antiseptic solutions over a period of years. Amphyl (morbidity 12.02 per cent) was administered in 707 cases; however, one vaginal examination was allowed in each case. The 10 per cent mercurochrome series (523 cases) showed a morbidity of 10.28 per cent, but the solution was used as an external spray only. In a study of 326 cases, 4 per cent aqueous mercurochrome was instilled, providing a decreased morbidity figure of 6.94 per cent. In the series previous to the present one, we studied 1,000 consecutive cases using "S. T. 37" hexylresorcinol solution with a morbidity figure of 7.0 per cent. The present study with the use of Bimerphen solution in 910 consecutive cases has, under present day difficulties, produced the excellent morbidity figure of 5.71 per cent.

Discussion

The figure of 5.71 per cent morbidity with the use of Bimerphen solution compares favorably with results obtained from other studies. It would appear from our data that three instillations of the solution prove most effective, but even when only one instillation was administered, the morbidity figures are significantly lower than when no antiseptic was used. Mayes,⁷ in a survey of 848 diplomates of the American Board of Obstetrics and Gynecology and a study of 236,295

hospital deliveries following the use of vaginal instillations, reports that 60.9 per cent of these individuals used some type of vaginal antiseptic prior to and during labor. From the survey, it was determined that 24 different antiseptic solutions were utilized in a total of 224,575 deliveries. It would appear that the choice of antiseptic is not so important as the fact that the procedure of vaginal instillations should be instituted. Morbidity figures from the many studies indicate a definite reduction following the use of antiseptic vaginal instillations.

One of the most practical features of Bimerphen solution, at the present time especially, is the nonstaining qualities of the material. We feel that this solution meets the requirements set up for an adequate vaginal antiseptic.

Conclusions

1. The routine use of vaginal instillations prior to delivery is a valuable procedure.
2. Bimerphen solution has been found to be at least as effective as other antiseptic solutions.
3. Bimerphen solution is safe for mother and child, is rapid in action, easy to apply, and is nonstaining.

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VITAMIN AND ENDOCRINE THERAPY IN NAUSEA AND VOMITING OF PREGNANCY

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THIS study is based on 100 cases of nausea in early pregnancy. All vomited one or more times each day.

Forty-three received pyridoxine hydrochloride (B_6) alone. The first patients treated received 50 mg. intravenously at a dose which was given as often as the nausea recurred. In some of them 50 mg., gave partial or no relief. They were given 100 mg., with better results. The results with the use of B_6 alone were:

| | Completely Relieved | Partially Relieved | Failure |
|---------------|------------------------|-----------------------|---------|
| Primigravidas | 17 | 6 | 2 |
| Multigravidas | 6 | 7 | 5 |
| Total | <hr/> 23 | <hr/> 13 | <hr/> 7 |

A very interesting feature was the disparity in results between the primigravidas and multigravidas.

The patient was counted completely relieved only if no nausea remained. If she experienced some relief but had residual nausea; the result was counted as partial. If the patient felt that she was not benefited or was undecided, the result was counted a failure. If relieved from the nausea but it later recurred between injections, this was counted successfully treated.

Sixty-six patients received B_1 and B_6 in combined doses. The initial doses were 50 mg. of each, but this was increased to 100 mg. of each, after the smaller dose had given indifferent results in some cases.

| | Complete Relief | Partial Relief | Failure |
|---------------|--------------------|-------------------|---------|
| Primigravidas | 31 | 6 | 2 |
| Multigravidas | 15 | 5 | 7 |
| Total | <hr/> 46 | <hr/> 11 | <hr/> 9 |

Of the patients who received B_1 and B_6 in combination, nine had previously received B_6 alone with little benefit.

In these nine patients, four were relieved by the administration of combined vitamins.

The five who failed to be relieved by combined vitamins were given adrenal cortex extract in daily doses of 2 c.c. subcutaneously. Three of these patients said that they felt decidedly better on this treatment and were able to retain food.

Since we failed in some of our early cases with 50 mg. doses of the vitamins, we adopted the procedure of giving both components in 100 mg. doses to patients who had marked nausea. There was often a lag period of 24 to 48 hours after the injection before the patient received maximum benefit.

To conserve drugs, we gave most patients injections only as dictated by the return of nausea.

Six patients were given B_6 in doses of 25 mg. a day orally for one to two weeks. Only two felt that they were definitely benefited, however, and two patients of this group were not relieved by intravenous administration.

Our results with the combined vitamins were even better comparatively than shown in the statistics because we adopted the practice of giving severe cases the combination without preliminary treatment with B_6 . The most spectacular results were in those patients who had been vomiting for some time, and probably had developed a definite thiamin deficiency.

Six of the 100 were classed as having pernicious nausea and vomiting of pregnancy. Three were multigravidas and three were primigravidas. The primigravidas and one of the multigravidas were completely relieved. Two of the multigravidas were not benefited by vitamins.

At present we have no adequate explanation for the difference in the results in multigravidas and primigravidas. As shown experimentally, rats that are deprived of pyridoxine die in fits and dogs develop anemia. Its role in human physiology has not been definitely proved, however, the animal experimentation point to it as linked with fat metabolism.

It has been established that thiamin is necessary in certain phases of carbohydrate metabolism. It is easily exhausted in vomiting. For this reason, the results in those people who have vomited for a considerable period are often dramatic. Its exhaustion also leads to the polyneuritis of pregnancy.

The adrenal extract had the following rationale for its use: (1) It is essential in metabolism of all classes of foods; (2) in the laboratory, it has been shown to increase the activity of thiamin. If the adrenals are not secreting properly, then essential links in the metabolic enzyme chain fail.

The number of patients treated with this preparation was too small to permit conclusions.

Summary

Forty-three patients received pyridoxine hydrochloride (B_6) in doses of 50 to 100 mg. intravenously. Of this group twenty-five were primigravidas and eighteen were multigravidas. Eighteen, or roughly three-fourths of the primigravidas were completely relieved, while only six, or one-third of the multigravidas were relieved. Of the seven complete failures, five were multigravidas.

Thirteen of the group had partial relief of which six were primigravidas and seven were multigravidas.

A total of sixty-six patients received combined doses of thiamin hydrochloride and pyridoxine hydrochloride in doses ranging from 50 mg. to 100 mg. of each. Of this group, nine had previously received pyridoxine alone with partial or no relief at all. In this group there were twenty-seven multigravidas and thirty-nine primigravidas.

Thirty-one of the primigravidas were completely relieved; there were two complete failures, while six others had varying degrees but definite relief.

Fifteen multigravidas were completely relieved and seven were not benefited, while five reported partial relief.

Five patients who were not benefited by vitamins were given adrenal cortex extract. The usual dose was 2 c.c. given subcutaneously at daily intervals. Three felt better and were able to retain food.

Conclusions

Thiamin hydrochloride and pyridoxine hydrochloride combined in doses of 100 mg. each, were superior to pyridoxine alone, or to doses of 50 mg. each of the two combined.

The medication was usually given intravenously. If the patient was not benefited by the first injection further treatment was usually futile.

The results in primigravidas were much better than in multigravidas regardless whether pyridoxine hydrochloride was given alone, or in combination with thiamin hydrochloride, for this we have no adequate explanation at present.

Five patients in whom the vitamin treatment failed were given an average daily dose of 2 c.c. of adrenal cortex extract for a few days. Three were able to maintain food when given this medication.

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FURTHER STUDIES ON INTRAUTERINE SULFANILAMIDE PACKS

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PREVIOUSLY this clinic has reported the first work with intra-uterine sulfanilamide packs.¹ The principles of intrauterine tamponade and the literature on the subject were reviewed in that paper. In summary, that report demonstrated the superiority of sulfa gauze over plain and iodoform gauze packing on three counts: reduced uterine bacterial contamination, lower morbidity rates, and improved genital hygiene.

Our studies were continued in order to ascertain the most satisfactory form of intrauterine pack for this purpose and to set up standards for commercial preparation.

Several factors required further consideration: (a) The length and size of the gauze, (b) the concentration of the sulfanilamide; (c) the physical state of the gauze, i.e., dry or moist; and (d) the method of preparation for preservation and dispensing. This report deals with a consideration of these factors.

Size of Gauze.—As would be expected in a study of this sort, the number of cases of atonic uteri available for packing was small. By the use of ether, and delaying the post-partum oxytocic, we were able to simulate this pathologic state. The gauze from which the pack was prepared was 5 yards long and 36 inches wide, folded into a 2½-inch pack and saturated with sulfanilamide. The uterus was packed by the previously described technique. The amount of gauze remaining was measured to determine the amount of packing required. In the 32 uteri packed in this study, the maximum length of the 16-fold 2½-inch gauze was slightly over 4 yards and the average was about 3 yards (Table I). Because these were not truly atonic uteri, it seems desirable to recommend a 5-yard pack to permit a good margin of safety.

The Concentration of Sulfanilamide.—The concentrations of sulfa would seem to be fixed by its solubility; however, by varying the preparation procedure, a supersaturated gauze can be made. A 10 per cent impregnation made available to us, yielded approximately 0.7 Gm. per yard. Thus, if one used only the average 3 yards of packing, the quantity of sulfa in contact with the uterine wall would be small. When the concentration was raised to 20 per cent (1.5 Gm./yd.), the gauze became quite stiff and was somewhat difficult to handle.

The packs were left in the uteri for 24 hours and a blood sample was taken at the time of removal. Bacteriologic studies of the previous report¹ demonstrated the bacteriostatic action of the sulfanilamide; consequently these studies were not repeated. Table I records the blood levels with the different types of gauze studied. The consistently

higher level of blood concentration in the 20 per cent pack is not related to the length of pack used; this indicates the advantage of the higher gauze saturation.

Moist Glycerin Packs.—In order to avoid the stiffness of the 20 per cent dry pack, studies were run with moist packs—using glycerin to retain moisture and increase sulfanilamide saturation. This permitted us to use the 20 per cent pack with 1.5 Gm. sulfa per yard. This preparation was very much easier to handle and greatly facilitated packing the uterine cavity.

As noted in Table I, the 20 per cent moist packs gave a slightly higher average blood level than the dry; we are not sure whether this was due simply to a higher concentration of sulfa, to the suspended state of the sulfa in the glycerin, or whether the greater ease of handling

TABLE I

| DRY | | | MOIST | | |
|--------------|----------------|-------------------------|---------------|----------------|-------------------------|
| CASE NO. | LENGTH OF PACK | BLOOD LEVEL 24 MG. % | CASE NO. | LENGTH OF PACK | BLOOD LEVEL 24 MG. % |
| 10% SULFA | | | | | |
| 4 | 3½ | 0.48 | 1 | 3 | 0.24 |
| 5 | 2 | 1.92 | 2 | 2 | 1.37 |
| 7 | 4 | 1.2 | 3 | 2 | 1.14 |
| 8 | 2¾ | 0.35 | 6 | 4 | 1.06 |
| 12 | 4¾ | 0.94 | 9 | | 2.05 |
| 15 | 2 | 1.44 | 16 | 3½ | 1.8 |
| | | | 17 | 2½ | 1.4 |
| | | | 23 | 3 | 2.06 |
| 6 Cases Avg. | 3.1 | 1.1 | 8 Cases Avg. | 2.7 | 1.4 |
| 20% SULFA | | | | | |
| 14 | 3½ | 1.78 | 10 | 2 | 1.25 |
| 18 | 3 | 1.14 | 11 | 3½ | 2.87 |
| 19 | 2½ | .95 | 20 | 3½ | 5.04 |
| 24 | 2 | 0.57 | 21 | 2½ | 4.2 |
| 25 | 4 | 2.84 | 22 | 4 | 2.78 |
| 29 | 2½ | 1.15 | 26 | 3 | 2.05 |
| 30 | 3 | 2.05 | 27 | 3 | 1.4 |
| 31 | 4 | 4.2 | 28 | 4 | 2.42 |
| | | | 32 | 4½ | 2.94 |
| | | | 33 | 4 | 2.46 |
| 8 Cases Avg. | 3 | 1.83 | 10 Cases Avg. | 3.3 | 2.74 |

permitted a more adequate packing of the uterus. The latter would seem to be true, for a slightly longer pack was used in the moist group than in the dry group.

We wondered regarding the effect of the moisture on the hemostatic action of the pack. No case of true atonic uteri with post-partum hemorrhage was encountered in this group. However, the moderate bleeding of the etherized nonstimulated (oxytocic) uterus was very adequately controlled; no difference could be noted in this regard in the two types of packs used.

Preservation.—In our earlier work, we prepared the packs as indicated and wrapped them in cloth for sterilization. This was not a permanent preparation, so we attempted to have available in the delivery room, dry sterile packs and sterile containers of sulfanilamide powder, thus permitting us to prepare the pack fresh as required. With

a frequently changing nursing and intern staff, much time was lost, which, in patients with hemorrhage might prove to be critical.

The experimental packs of this study were supplied to us in small glass jars with sealed and clamped tops. This preparation permitted the pack to remain moist for periods up to eight months after fabrication. The pack remained pliable and the sulfa was not precipitated out. On checkup, the 20 per cent gauze still contained approximately 1.5 Gm. per yard.

Summary

In both the present and previous study the morbidity, in terms of temperature elevation over 100.4° F. was surprisingly low. Fear of infection has frequently been responsible for undue delay in packing a bleeding, atonic uterus. With the great reduction in morbidity and infection resulting from the addition of sulfanilamide to the pack, its early use in the control of hemorrhage is to be recommended.

This study is a continuation of work on sulfanilamide impregnated gauze for uterine packs and reports on the physical features of such packs.

From these studies we believe a glycerin 20 per cent sulfanilamide gauze made up as a 2½-inch (16-fold) by 5-yard roll, prepared in a sealed glass container is the most satisfactory pack for intrauterine tamponade for use in the average hospital delivery room.

The experimental packs used in this study were prepared by the Johnson & Johnson Research Foundation, New Brunswick, N. J.

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ECLAMPSIA WITHOUT CONVULSIONS, HYPERTENSION OR COMA

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ECLAMPSIA without convulsions is rare. Slemons² reported 9 cases, the last two in 1907. Coffiere³ reviewed the literature up to 1927 and found 38 cases. The last discussion of this condition appeared in 1933 by Arthur G. King⁴ who reported the forty-fourth case. However, Dieckmann¹ mentions another case in his book *Toxemias of Pregnancy*. Other cases have undoubtedly been undiagnosed because of lack of necropsy evidence or have not been recorded in the literature.

Eclampsia without convulsions, or coma, is extremely rare. Wegner and Dieckmann reported the eighth such case in 1932. The diagnosis was made at autopsy which revealed the presence in the liver of periportal hemorrhages, anemic infarcts or thrombosis of the portal vein.

Cruickshank, Hewitt and Couper reported that 18 per cent of their eclamptic patients had blood pressures less than 141 mm. of Hg. while 22 per cent were over 200 mm. Hg, the mean being 168 mm. Hg. Herson found that 95 per cent of his eclamptic patients had a systolic pressure over 136 mm. Hg.

Eighty-five per cent of eclamptic patients reveal edema of legs and almost 100 per cent have either latent or demonstrable edema.

The following is a report of eclampsia without convulsion, hypertension, edema or coma.

Mrs. L. G., a primigravida, aged 29 years, and at term November 22, 1943, presented herself for examination June 10, 1943. Her past history was irrelevant; blood pressure was 110/80, uterus size of 14 weeks' gestation; urine negative, weight 105 pounds.

The essential data of subsequent office visits are as follows:

| | UTERUS | BLOOD PRESSURE | URINE | WEIGHT |
|--------|----------|----------------|----------|--------|
| 7/8/43 | 18 weeks | 112/80 | negative | 107½ |
| 8/5/43 | 22 weeks | 130/86 | negative | 108¾ |
| 9/2/43 | 26 weeks | 136/84 | negative | 111½ |

On 9/16/43 her blood pressure was 145/90, uterus 28 weeks in size, weight 111½. Patient remarked she was emotionally disturbed due to her husband's eventual entrance into the Army. She was told to remain at bed rest and return in one week. On 9/23/43 she was feeling well again, her blood pressure being 140/88, and her weight 112½. The uterus seemed smaller (size of 26 weeks), but the fetal heart sounds were good. She was placed on a low protein, salt-free diet, and bed rest. One week later, 9/29/43, the uterus was the size of 26 weeks, blood pressure was 130/80, and the urine contained one-plus albumin. She was seen again on 10/13/43 with no subjective complaints. The uterus was now the size of 24 weeks' gestation, fetal heart sounds good, blood pressure 150/88, urine ++ albumin, and her weight was 114½ pounds. Patient was told to continue diet and bed rest and report in one week.

*Presented at a meeting of the Chicago Gynecological Society, December 17, 1943.

Four days later, on 10/17/43, at 12:30 P.M., the patient phoned and complained of mild epigastric distress. She was told to remain at bed rest and apply heat over the epigastrium. At 2:30 P.M. patient again phoned stating that the pain was more severe and associated with mild nausea. Paregoric was then prescribed. At 4:00 P.M. she again phoned and stated that pain was now very sharp and radiated to back and right shoulder and was associated with nausea and vomiting. She was seen at 4:30 by one of us, and found to be doubled up with pain, sharp in character, radiating to the back and right shoulder. She had emesis at this time and the vomitus contained bile. There was slight rigidity over the right upper quadrant associated with marked tenderness to pressure over the gall bladder area. Her pulse was 80, blood pressure was 128/86, no edema present and she was fully alert. A diagnosis of biliary colic was made and morphine sulfate gr. $\frac{1}{4}$ was administered. By 5:15, she was more comfortable. At 7:15, an urgent phone call was received stating that she had fainted and did not respond. The breathing was deep and stertorous. At 7:40 when one of us arrived at the home, death had just occurred. On questioning the attendants, it was learned that she suddenly did not respond to questioning, but no convulsions were noted at any time. An autopsy was performed on 10/18/43 by Dr. Otto Saphir, pathologist of Michael Reese Hospital, revealing the following essential findings:

"The liver is enlarged and presents a mottled appearance, the mottling being caused by large areas of hemorrhage which vary in size from one or two millimeters to a few centimeters in diameter. Many of the latter are fused by confluence. This is particularly marked in the region of the diaphragmatic surface of the right lobe. On section, similar areas are found on the cut surface. The interliver tissue shows distended central zones. Within the region of the hemorrhages the liver tissue is not recognizable, but appears to be necrotic. The gall bladder contains a small amount of thin liquid bile. The bile passages are patent. Neither the branches of the hepatic veins, which are carefully dissected, nor the branches of the portal vein show any noteworthy change.

The kidneys are of a greenish, grayish, brown color. The capsule scrapes away with ease, leaving a smooth surface. On section, the architecture of the cortex is somewhat obscured, but otherwise no changes are noted.

The vagina and cervix appear normal. The uterus corresponds to about seven months of pregnancy. When the uterus was opened, it was found that the fetal sac was devoid of any fluid. The placenta was firmly attached to the uterus and the membranes were also attached to the mucosa of the uterus. The fetus measures 35 cm. in length. No changes in the organs examined were noted, externally and internally.

Microscopic Findings.---

Liver: There are large areas of hemorrhages which are invaded by many polymorphonuclear leucocytes. There is a considerable necrosis seen in these regions. These areas are situated predominantly in the regions of the periportal spaces while often the central zones show no changes with the exception of a moderate cloudy swelling of the lining cells. Often a small bile duct is noted practically completed, surrounded by an area of necrosis, with red blood corpuscles and a few polymorphonuclear leucocytes. Though blood vessels cannot be defi-



Fig. 1.—Eclamptic liver: Note the enlargement due to the presence of subcapsular hemorrhages, most pronounced along entire diaphragmatic surface.

nately identified in the necrotic regions, it seems that some of the larger veins are involved. They show evidence of necrosis in at least some portions of their walls.

The outstanding changes in the kidney are a rather severe cloudy swelling involving the lining cells of the convoluted tubules, and also a number of lining cells of connecting tubules. The lumina of the latter contain much of a reddish, granular material. The glomeruli show no changes with hematoxylin-eosin stain. However, a MacGregor preparation reveals that the basal membranes are distinctly thicker than normal and sometimes appear smudgy. A number of arterioles show no changes. An occasional small blood vessel—it cannot be decided whether this is a vein or not—shows necrotic walls. Here and there the Goormaghtigh (juxtaglomerular) apparatus is recognized but no changes are elicited.

The uterus shows typical changes of pregnancy. The placenta shows several large infarcts, the villi perhaps slightly smaller than normal, but all of them show open blood vessels.

Pathological Diagnosis.—

1. Eclamptic liver

Cloudy swelling of the myocardium and kidneys

Petechial hemorrhages in the endocardium

Pregnant uterus with about 7-month-old fetus

Absence of amniotic fluid

Edema of lungs.

In conclusion, the case is both rare and interesting because of the following:

1. It demonstrates eclampsia without convulsions, and questionable coma.

2. A normal blood pressure was associated with the eclampsia while prior to the episode there was a slight to moderate hypertension.

3. The absence of visual and latent edema in the presence of eclampsia

4. The possible relationship between absence of amniotic fluid to the above toxemia.

5. Acute involvement of liver with little or no involvement of kidneys and other organs.

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REPORT OF 67 CONSECUTIVE POST-PARTUM STERILIZATIONS

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SINCE 1940, sixty-seven post-partum sterilizations have been done at the Louisville General Hospital. The Madlener technique with some minor modifications has been employed. Not included in this series are twenty-four Madlener sterilizations done at the time of cesarean section. Sixty-three cases were sterilized within twenty-four hours, two cases after twenty-nine hours, one case thirty-one hours after delivery, and one was done on the tenth post-partum day.

In this series we have fifty-three cases that were delivered spontaneously, two that were delivered spontaneously with an episiotomy, three delivered by low forceps, three delivered by episiotomy and low forceps, five by breech extraction, and one by podalic version. There were four sets of twins.

In this paper we are reporting the use of local anesthesia, a transverse incision, the crushing of the Fallopian tubes close to the cornu of the uterus, and a silk-suture closure of the abdominal wall. We are also presenting additional evidence that post-partum sterilizations do not cause an increase in puerperal morbidity if done within twenty-four hours after delivery.

Technique

The present policy of the department does not allow a sterilization to be performed if the patient is more than twenty-four hours post partum.

We are employing local anesthesia using 150 to 200 c.c. of 0.5 per cent novocain with 0.2 c.c. of adrenalin per 100 c.c. of novocain. Two hours before operation, the patient is given three grains of nembutal, and morphine and scopolamine are given twenty minutes preoperatively. Adair and Brown¹ report the use of local anesthesia, and we have also found this method adequate and comfortable for the patient.

Except for a few modifications, we use the same technique as followed by Adair and Brown.¹ Instead of a longitudinal incision, we have been using a 2 to 2½ inch transverse incision of the skin and anterior sheath of the rectus. The muscle itself is retracted and very often the diastasis recti affords easy retraction. The posterior sheath and peritoneum are incised transversely in turn. The incision is made over the fundus of the uterus. We believe that this facilitates seizure of the Fallopian tubes with a Babcock clamp. After we identify the tube by tracing it to its fimbriated end, it is crushed in two places by a single application of a Kelly clamp. One of these crushed areas is always two centimeters from the cornu of the uterus. We crush the tubes close to the cornu in order to prevent conception through accessory ostia. For the double ligation we use heavy braided silk. In all our recent cases, silk has been used to close the abdominal wall.

In this series there were thirty-four transverse incisions, most of which were done in the last two years. A silk closure was used on thirty-nine cases. None of our wounds have been infected.

Indications

The decision for sterilization of all but the mental cases rests with the department of obstetrics and gynecology. All mental cases have to be passed by the department of psychiatry. The following chart shows the indications for sterilization in this series:

| | |
|--|----|
| <i>Toxemia</i> | |
| - All types of recurrent toxemia | 22 |
| <i>Heart Disease</i> | |
| Hypertensive cardiovascular | 8 |
| Rheumatic | 2 |
| <i>Mental Disease</i> | |
| Feeble-minded | 8 |
| Schizophrenia | 2 |
| Manic depressive | 2 |
| <i>Orthopedic</i> | |
| Ankylosis of left hip and knee | 1 |
| Mid thigh amputation | 1 |
| <i>Lung Disease</i> | |
| Moderately advanced tuberculosis | 1 |
| Far advanced tuberculosis | 1 |
| Tuberculous effusion | 1 |
| <i>Metabolic Disease</i> | |
| Diabetes | 2 |
| <i>Varicosities</i> | |
| Varicose veins of legs and vulva | 2 |
| <i>Renal Disease</i> | |
| Bilateral hydronephrosis | 1 |
| Recurrent pyelitis | 1 |
| Nephrosis | 1 |
| <i>Miscellaneous</i> | |
| Phlegmasia alba dolens | 1 |
| G.N.S. (syphilis) | 1 |
| Pelvic disproportion with previous section | 1 |
| Multiparity | 8 |
| Total | 67 |

Post-partum Interval

Of the sixty-three cases done within twenty-four hours, the longest interval was twenty-two hours and the shortest interval was one hour. Sixteen cases were done in five hours or less. Twenty cases were sterilized between five and twelve hours. Twenty-six patients were sterilized between twelve and twenty-four hours. Two cases were sterilized after twenty-nine hours, and one case was done after thirty-one hours. One case was sterilized on the tenth post-partum day. The average interval for sixty-three cases done within twenty-four hours was 11.4 hours. For all cases exclusive of the case done on the tenth day, the average interval was 12.3 hours.

Morbidity

Our percentage morbidity was 2.9 per cent or two cases. This compares with the morbidity reports of Adair and Brown,¹ Hewitt and Whitley,⁴ Birch,⁷ and Lock, Forman and Webster.⁵ There were no mortalities. Herewith is a review of the two morbid cases.

CASE 1.—(7802.) Gravid^a xv, para xiv. The post-partum interval was twelve hours following a spontaneous delivery of twins. At the time of operation the surgeon discovered many adhesions between the omentum and peritoneum. In order to reach the tubes, he found it necessary to incise an avascular portion of the omentum. He later repaired the omentum with chromic catgut. The abdomen was closed with catgut. This patient was classified as morbid for she had a temperature of 100.4° F. on her seventh postoperative day, and 100.6° F. on her eighth postoperative day. No cause for the fever was ascertained.

CASE 2.—(70751.) Gravid^a i, para 0. This patient was delivered spontaneously following an episiotomy. The post-partum interval was ten hours. Her prenatal record showed that she was treated for a mild pyelitis during her twentieth week of pregnancy. This patient arrived in the operating room with a temperature of 100.4° F. After the abdomen was opened a full bladder was found, and the operator decided that the patient had to be catheterized before he could resume the procedure. On the third day, the patient had a temperature of 101° F., and complained of her episiotomy hurting. On the fourth day the temperature was 101.2° F., but a catheterized urine specimen showed no findings consistent with a urinary tract infection. She had no subjective symptoms of pyelitis. At no time was her episiotomy broken down or infected. The patient was started on sulfathiazole on her fifth day and was completely afebrile on her eleventh.

Postoperative Stay

The average postoperative stay was 10.2 days for sixty-five cases. One patient stayed on for treatment of her diabetes, and another was retained by the department of psychiatry. Forty-two cases left the hospital on their tenth day or less. Up until last year most patients stayed 10 to 12 days. Now they are discharged on their ninth or tenth postoperative day.

Summary

Sixty-seven consecutive cases of post-partum sterilizations have been reviewed. With some minor changes, the Madlener technique as reported by Adair and Brown¹ has been used. The usage of local anesthesia, a transverse incision and crushing of the tube two centimeters from the cornu uteri is recommended. We believe that this is a safe procedure if done within twenty-four hours after delivery. Notwithstanding the fact we have reported fourteen cases that have had some obstetric intervention, we believe that there will be little risk with cases that deliver spontaneously. The operative procedure does not prolong the hospital stay beyond the regular post-partum stay, nor is there any increase in the puerperal morbidity.

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BRENNER TUMOR OF THE OVARY ASSOCIATED WITH SARCOMATOUS CHANGE IN FIBROMYOMATA UTERI

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THE perplexing problem that is involved in the classification of ovarian tumors is almost overwhelming when one glances at the outline that was offered some 15 years ago. Now, thanks to the continued study by pathologists and constant reporting of cases in the literature by clinicians, a clearer understanding is gradually evolving. It is with this in mind that we present this case report, hoping it may in some way contribute further evidence.

In 1907, Brenner¹ first described the type of tumor we are presenting but called it oöphoroma folliculare. He made no differentiation from the granulosa cell growths and it was not until 1932 that Robert Meyer² sharply distinguished between the two. Since then various authors, Novak, von Szathmáry and Varangot, have reported groups of cases and reviewed the literature. The total number of cases now approaches 130.

The case we offer is quite typical both clinically and pathologically and is unusual only in that it is associated with a fibromyoma of the uterus which showed sarcomatous degeneration. The symptoms which eventually drove the patient to her physician were excited by the tumor making contact with the cecum and the bleeding caused by the fibromyoma. How long the Brenner tumor had existed, or how long it would have persisted had some adjacent structure not become involved, cannot be answered.

Case Report

Mrs. W. A. R., 51 years old, was first seen on December 7, 1942, at which time she complained of the following: (1) R.L.Q. pain and tenderness, which at times was excruciating but did not cause nausea or vomiting—four weeks' duration. (2) Loss of ten pounds in weight. (3) A daily temperature elevation between 99 and 100 degrees F. of two weeks' duration. (4) Vaginal bleeding requiring one or two pads daily, of seven months' duration.

Her menses first began at the age of 12, were regular every 28 days, lasted 4 to 5 days and were always associated with pain on the first day. In 1940, her periods became irregular and the amount of bleeding was variable. Hot flashes were intense. Periods ceased in November, 1941, and she had no discharge or flow until April, 1942, when the present illness began.

Her only pregnancy occurred at the age of 25, and terminated in a 2½ months' complete abortion. She gave a history of having been treated for arthritis in the left hand in 1931. Had pneumonia in 1936 and afterward, received treatment for hypertension and bradycardia.

Physical examination revealed a white, short, obese, pale female. T. 99.6° F., P. 90, B.P. 140/90. Lungs were clear. Heart tones were of

good quality and rate was regular. The abdomen was thick walled and tender in the entire lower portion but particularly on the right side where a mass was questionably outlined. The vaginal outlet was marital and cervix normal. The uterus was tender, irregular and enlarged upward and laterally toward the cecum. Bimanual examination was not entirely satisfactory because of the obesity and tenderness. A probe showed the uterine canal to be $3\frac{1}{2}$ inches in length and somewhat irregular. This maneuver caused an increase in the bleeding.

Provisional Diagnosis.—Large fibromyoma of the uterus with degeneration and possible early carcinoma of the fundus.

The patient was referred to the hospital December 10, 1942. X-ray examination of heart and lungs was essentially negative except for elevation of the right side of the diaphragm. X-ray study of the gastrointestinal tract was interpreted as follows: "Mass lesion of the pelvis causing deformity of the cecum from extrinsic pressure; displacement of the sigmoid due to same; displacement of the small intestine from the pelvis."

Laboratory Report: R.B.C. 4,640,000. W.B.C. 11,650. Hemoglobin 86 per cent. Two urinalyses were normal.

Operation was performed on December 15, 1942. Curettage revealed no endometrial tissue. The abdomen was opened by a right paramedian incision, revealing a large ovoid-shaped ovarian cyst. Its origin was from the left adnexa and its right pole was adherent to the cecum by fibrin and fibrinous bands. The cyst was easily freed from the bowel and was found definitely to be of solid structure at the point of contact. This was the portion which showed the Brenner tumor.

The tumor and left tube were removed and a panhysterectomy and right salpingo-oophorectomy were performed. The uterus showed a 4 to 5 cm. fibroid at left cornu. There was no evidence of invasion or glandular enlargement.

The postoperative course was normal, the patient being discharged on December 29, 1942.

Pathologic Examination.—The left ovarian tumor is 13 cm. in diameter. In one pole there is a solid area 5 cm. in diameter. From the inner surface of this solid portion there is a soft, papillary mass projecting into a cyst, the latter being 8 cm. in diameter. The solid area cuts with increased resistance and the cut surface shows small cysts and an occasional area of hemorrhage.

Sections from the solid portion show numerous nests of typical Brenner cells. Where well preserved, the tumor cells are polyhedral, flat and arranged in circumscribed or elongated masses. In all cases the tumor cells are surrounded with dense fibrous tissue. Many of the tumor nests show degenerative changes and are lined with a single layer of cuboidal or flat cells. Frequently epithelial remnants are seen in the center of these degenerated nests.

Sections from areas adjacent to the papillary growth show more extensive degeneration of the Brenner tumor nests. Here there is a greater tendency to elongation and the lining cells become more columnar. In the fully developed, pseudomucinous area, the tumor cells surround papillary strands of vascularized connective tissue stroma. The cells become more cylindrical and are usually one layer in thickness. Cilia were not noted in either the pseudomucinous structure, or solid area. Many Brenner tumor-cell nests are present in the stroma of the pseudomucinous growth.

Sections of the soft Leiomyoma in the uterus show it to be very cellular. The tumor cells are atypical, variable in size and both round and spindly in shape. Mitotic figures are fairly numerous.

Follow-up.—The patient was last seen on March 5, 1944. She was feeling well. Hot flashes were controlled by Premarin. Abdominal wound and vault were well healed. There was only slight pelvic tenderness and no masses.

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SPONTANEOUS POST-PARTUM DISAPPEARANCE OF MASSIVE CONDYLOMATA ACUMINATA OF THE VULVA

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CONDYLOMATA acuminata of the perineum, vulva, vagina and cervix are seen not infrequently among those pregnant women with a profuse vaginal discharge. Recently radium¹ has been used to treat small warts of the vulva soon after delivery.

The object is reporting this case is to re-emphasize the possibility of complete spontaneous disappearance of massive condylomata acuminata of the vulva after delivery.

The patient, a 23-year-old gravida iii, para ii, entered the San Francisco City and County Hospital Prenatal Clinic March 24, 1942. Her last menstrual period was December 23, 1941, and the expected date of confinement was September 30, 1942. Her course was uneventful until July 21, 1942, when she presented herself at the clinic with the complaint of itching warts of the vulva for several weeks. On examination, the major and minor labia were found to be covered with multiple minute papillomata and there was a 1-centimeter condyloma at the fourchette (Fig. 1). She was sent into the hospital where under caudal-block anesthesia with 40 cubic centimeters of 1 per cent procaine hydrochloride, the growth was excised from the fourchette and the remainder of the warts were removed and the bases cauterized with the actual cautery. Petroleum jelly was applied to the cauterized areas.

The patient failed to report again to the clinic for examination until 3 weeks before confinement. At that time, there was a 6-centimeter warty growth involving both minor labia. Only a minute recurrence was present at the fourchette. Because of the closeness to term, it was considered inadvisable to exercise or cauterize the tumor. The patient was told to wash the area several times each day with plain water and to keep the growth thoroughly dried at all other times. She re-entered the hospital October 2, 1942, and delivered spontaneously after a 2-hour labor assisted only by a right medio-lateral episiotomy. The labial growth did not interfere with the delivery and there was no bleeding from it.

The post-partum course was afebrile and the patient was dismissed on the tenth day with the advice that she keep the vulva clean and dry. It was planned to wait several weeks before instituting any specific treatment to eradicate the growth. The warts rapidly diminished in size until 8 weeks post partum, at which time there remained only a 3-millimeter nodule just below the fourchette and a 1-centimeter group of nodules on the lateral surface of the right minor labium. Still without any therapy other than cleanliness and dryness, the warts completely disappeared by January 9, 1943, 14 weeks post partum.

The Wassermann reaction was negative and smears taken from the urethra and cervix were negative for gram-negative diplococci. No *Trichomonas vaginalis* were found. A few mycelia were present at the first examination of the vaginal discharge, but none were found thereafter.

Conclusions

During the first two trimesters of pregnancy, condylomata acuminata of the vulva, vagina and cervix should be treated by excision and cauterization. Recurrences frequently occur and can be effectively con-

trolled by frequent cauterizations, coupled with measures to decrease the discharge which is usually present.

The problem in the latter part of the third trimester, must be approached in a different manner. Because of the imminence of labor and the increased vascularity of the tissues and the tumor, excision or



Fig. 1.—Pregnancy at 7 months. Multiple small condylomata acuminata of the major and minor labia and a 1-centimeter papilloma at the fourchette.

cauterization is inadvisable. In addition, there is always a possibility of increasing the chances of infection. Under these circumstances, I consider it preferable to take measures to control the discharge from the vagina and the infection of the tumor, and to deliver the patient by the most appropriate means. If the infection has been effectively checked and the tumor does not, as in the present case, offer an obstruction to delivery, she should be delivered from below. However, should the tumor be large and ulcerated, or involving the perineum to an appreciable extent, then extraperitoneal cesarean section has to be considered seriously as offering the lesser hazard to the patient.

After delivery the major hazard to the patient has passed, and she may be observed for a period of weeks during which time cleanliness is stressed. Radium, x-ray, cauterization or excision should be reserved for those cases that show no evidence of regression after 3 to 4 weeks.

Before attempting to evaluate the efficacy of any method of treating these lesions, cognizance must be taken of the fact that spontaneous disappearance of condylomata acuminata does occur after delivery.

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PRIMARY OVARIAN PREGNANCY

Report of Three Cases

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IN THE past 24 years there have been 206 cases of ectopic pregnancy at this hospital. Primary ovarian pregnancy has occurred in three instances of this series. These will be described below. Mercer,¹ in 1614, suggested that such an occurrence was possible and since that time there have been approximately 120 cases reported in the literature. However, an authentic case must fulfill the widely quoted criteria proposed by Spiegelberger. These are: 1. An intact and normal uterine tube of that side. 2. Connection of the pregnancy mass to the uterus by the uteroovarian ligament. 3. That the gestation sac occupy the position of the ovary. 4. That there be unquestionable ovarian tissue in the wall of the sac. According to Meyer and Wynne,² the first authentic cases are those of Kauwer in 1897 and Tussenbroeck in 1899. Thomas,³ in June, 1943, set the number of authentic cases at 65.

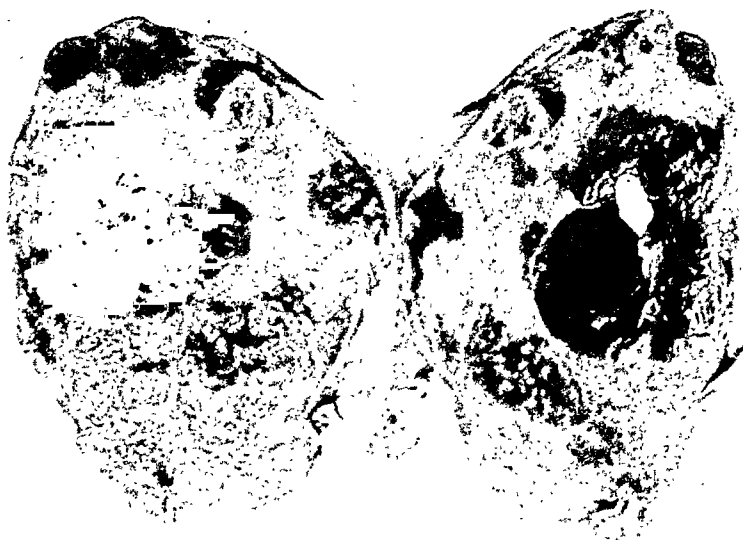


Fig. 1.—(Case 1.) Gross specimen on hemisection. Note centrally located gestation sac, embryo and deeply hemorrhagic ovary. Between the two halves of the ovary is the stump of the uteroovarian ligament. ($\times 1.2$.)

CASE 1.—(Service of Dr. O. R. Lillie.)

E. V., a white female, 20 years of age, married, gravida 0, admitted to the hospital January 8, 1944 because of pain in the right lower quadrant. The pain began one week prior to the admission. In November, 1943, the patient had her last normal menstrual period. Subsequently irregular episodes of bleeding persisted for three weeks. On admission, physical examination was negative except for tenderness in the right lower quadrant and a palpable mass in the right adnexal region. In the early part of January, 1944, the Friedman test was posi-

tive. At laparotomy, the internal genitalia, with the exception of the right ovary, were found to be normal. Both uterine tubes were without gross change. The right ovary, which was in its normal position and attached to the uterus by the uteroovarian ligament, measured 6 by 4 by 4 cm. On section of the ovarian mass, there was encountered a centrally located 22 mm. cavity filled with a clear, watery fluid. A well-developed 8 mm. embryo was attached to the wall of this cavity. The head and eyes, the cardiac protuberance, and the limb buds of the embryo were clearly visible (Fig. 1). The major share of the ovarian substance around the gestation sac was deeply hemorrhagic. Microscopic examination of the hemorrhagic ovarian tissue revealed the presence of chorionic villi. No decidual tissue was found in the sections of the ovary.

CASE 2.—(Service of Dr. A. H. Lahmann.)

H. H., a 24-year-old white, married female, gravida 0, admitted to the hospital July 21, 1941 because of bleeding for four days prior to entrance. The last normal menstrual period occurred on May 17, 1941. The patient was a known cardiac invalid with a severe rheumatic mitral stenosis. Pelvic examination revealed a mass in the right adnexa. The Friedman test at this time was positive. Dilatation and curettage was performed and a microscopic diagnosis of "decidual tissue" was made. Five days later, a right salpingo-oophorectomy was performed. The specimen measured 7 by 5 by 3 cm. and weighed 50 grams. The tube was average in size and upon opening was found to be entirely normal. The ovarian mass revealed a centrally located 10 mm. sac outlined by a smooth, glistening membrane and surrounded by deeply hemorrhagic tissue. The uteroovarian ligament was attached to the specimen of ovary.

Microscopic examination of the ovarian tissue revealed the presence of chorionic villi and decidual cells. No embryo was found in this case.

CASE 3.—(Service of Dr. R. S. Cron.)

W. M., a 23-year-old married, white female, gravida 0, admitted to the hospital May 16, 1940 because of nausea, vomiting and vaginal bleeding appearing on the day of admission. One and one-half months prior to admission, the patient experienced pain in the lower part of the abdomen, and irregular vaginal bleeding. A Friedman test done at that time was positive. Corpus luteum extract was administered and the patient was confined to bed for one month.

In four years of married life she had not conceived. One year previously, a complete study was performed because of sterility. Menstrual history, however, was regular.

Physical examination was essentially negative except for tenderness in the left lower quadrant and a palpable mass in the left adnexal region. At laparotomy a large mass was found occupying the position of the left ovary. This was attached to the uterus by the uteroovarian ligament. The left uterine tube was not removed and was described as normal. The ovarian specimen measured 8 by 7 by 4 cm. One part of the specimen was occupied by a clear serous cyst measuring 4.5 cm. in diameter; the balance was made up of coagulated blood measuring 5 cm. No sac or embryo was found in this specimen. Microscopic examination of the ovarian substance and coagulated blood showed the presence of a corpus luteum and chorionic villi. Other findings at the time of surgery revealed a corpus hemorrhagicum of the right ovary and endometrial transplants in the posterior cul-de-sac.

Comment

The mechanism by which the ovary comes to bear the dividing and developing ovum is a matter of speculation. The most probable theory is that of fertilization of the normal ovum within its follicle. Spermatozoa may reach the surface of the ovary and fertilize an ovum within a recently ruptured Graafian follicle. Sterility is a rather common factor in the cases of the ovarian pregnancy. The three cases reported herein had not been gravid prior to the occurrence of ovarian pregnancy. Wollner,⁴ also stresses the factor of previous sterility and suggests that there may be some inherent defect in ovulation. On the other hand, Curtis⁵ believes that it is possible for a normally fertilized ovum (in the tube) to lose its "traction" and slide back into a recently ruptured Graafian follicle wherein nidation may take place. Finally, nidation may take place in other epithelial structures such as endometrial implants or Müllerian duct remnants on the surface of the ovary. Cron⁶ has noted a case of ectopic pregnancy in an endometrial implant on the surface of the rectum. It is his opinion that in Case 3, the ovarian pregnancy developed in an area of endometriosis.

Summary

Three cases of primary ovarian pregnancy are presented. All are authentic according to the classification of Spiegelberg. Pregnancy had not occurred in these individuals prior to the development of ovarian gestation. Fertilization of the ovum within its follicle is the probable mechanism in Cases 1 and 2. In the third case, pregnancy evidently had taken place on the surface of the ovary in an endometrial implant.

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THECOMA OF THE OVARY WITH ASCITES AND HYDROTHORAX (MEIGS' SYNDROME)

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*(From the Section on Obstetrics and Gynecology, Ochsner Clinic and
Touro Infirmary)*

ALTHOUGH fibroma of the ovary associated with ascites and hydrothorax was reported as early as 1879 by Cullingworth,¹ it was not until 1937 that the condition was recognized as a clinical entity when it was described by Meigs and Cass.² The syndrome is not common; only 30 cases had been recorded by January 1943, according to Meigs and his associates,² who collected the cases reported in the literature. There have been patients undoubtedly, exhibiting this symptom complex who were considered to have inoperable malignancies, and who were treated only palliatively. The condition can be cured only by surgical removal of the tumor. Therefore, it is important to familiarize the medical profession with this syndrome so that they may consider it in the differential diagnosis when a patient is seen with fluid in the abdomen and chest, and institute surgical treatment as soon as the condition is recognized.

The mechanism of formation of ascites and pleural effusion associated with ovarian tumors remains speculative. It has been ascribed to the "shocking" action of the tumor, torsion of the pedicles of the tumor, the presence of pleuroperitoneal tubes and to penetration via the diaphragmatic lymphatics.¹

Although this syndrome may appear at any age, most of the reported cases have occurred following the menopause. The clinical picture is not characteristic and often simulates a pelvic malignancy with metastases. The symptoms may be referable primarily to the presence of fluid in the chest, or they may be only suggestive of the pelvic mass. The patient may complain of gastrointestinal disturbances such as cachexia and loss of weight, and of dyspnea, abnormal vaginal bleeding, and menstrual difficulties.

The rarity of Meigs' syndrome would appear to justify the report of another case. Whereas most of the reported cases have been fibromas, this is a case of thecoma of the ovary associated with ascites and hydrothorax. Since the patient was under observation before any evidence of ascites and hydrothorax appeared, this case demonstrates how rapidly fluid may accumulate in the peritoneal and pleural space, a point which Meigs had emphasized.

Miss O. W., white, aged 44, came to the clinic April 30, 1942 with a complaint of leucorrhea. Vaginal examination revealed a hard, apparently fixed mass which was attached to the posterior surface of the uterus on the left. A small cervical polyp was cauterized, following which the leucorrheal discharge disappeared.

On June 25, 1943, fourteen months after the patient was first seen, she returned because of abdominal distention and pain. She had not menstruated for six or eight months, but had not noted any pronounced menopausal symptoms.

Abdominal palpation revealed a gaseous distention and pain on manipulation. On vaginal examination, a mass the size of an orange was felt in the pelvis. The mass could not be lifted out and was somewhat sensitive on manipulation.

Roentgenograms of the chest on June 29, 1943, revealed haziness in the right base which was interpreted as due to a thickened pleura.

It was considered advisable to observe the patient for a while. She returned ten days later at which time the mass had definitely increased in size and its removal was advised.

The patient was admitted to Touro Infirmary July 6, 1943. For one week before entrance to the hospital, she had had diarrhea. She also complained of a feeling of tightness in the abdomen and severe backache. For several days before admission, she could hear splashing noises in her abdomen when she moved. For four days prior to admission, she had a slight nonproductive cough and slight dyspnea with a sense of fullness in her chest.

Examination of the chest revealed flatness to the level of the eighth rib over the right base. No breath sounds could be heard and tactile fremitus was absent. Immediately above this area, fine crepitant râles could be heard. The heart appeared to be slightly enlarged to the left with a normal rate and no murmurs. The abdomen was protuberant and symmetrically enlarged. The skin was tense. Percussion revealed dullness and flatness in the dependent portions of the abdomen. Shifting dullness and a fluid wave were demonstrated. No masses could be felt. The liver and spleen were not palpable. The only significant finding on vaginal examination was a mass in the left adnexal region which was interpreted as an ovarian tumor.

On July 7, 1943, under a general anesthetic, a laparotomy was performed. Approximately one gallon of amber colored fluid was found in the peritoneal cavity. Exploration of the pelvis revealed a solid tumor of the left ovary, which was attached to the posterior peritoneum, filling the cul-de-sac and the posterior surface of the broad ligament. A small fibroid was felt in the uterus. A bilateral salpingo-oophorectomy and total hysterectomy were performed.

The pathologic report showed a tumor of the left ovary measuring 12 cm. by 7 cm. by 7 cm. The external surface was covered by a firm membrane and was grayish-white in color except for several areas of golden yellow. Section revealed a cut surface which varied in color from light reddish-brown to golden yellow. The golden-yellow color was intermingled in island-like formations within the general surface which appeared to be from grayish-white to light reddish brown. The tumor was fairly firm in consistency but showed several local areas which were soft and were golden-yellow in color. The uterus and cervix measured 6 cm. by 3½ cm. by 2½ cm. The endometrial cavity was normal in contour. The myometrial wall revealed several intramural leiomyomas. The cervix contained an endocervical polyp measuring 2 cm. by 4 cm. by 1 cm. The tubes were densely adherent to the ovaries and the fibrinated ends were not patent. The right ovary revealed a ruptured follicular cyst on one pole.

The microscopic diagnoses were thecoma of the ovary, follicular cysts of the ovary, chronic salpingitis, intramural leiomyomas, chronic cervicitis and endocervicitis and benign endocervical polyp.

The patient's convalescence was uneventful. Examination of the chest on July 12, 1943, revealed a Gracca's triangle at the right base extending to the sixth dorsal vertebra. No fluid was demonstrable in the abdomen. By July 15, 1943, evidence of pleural fluid was almost gone; there was a suggestion of a small amount of fluid at the right base posteriorly near the mediastinum. The breath sounds were diminished and tactile fremitus decreased over the right base.

Follow-Up Examination.—On July 30, 1943, a small amount of fluid was noted in the right base of the thorax. On August 23, 1943, pelvic examination was negative. No fluid was found in the abdomen. The patient had no complaints and was discharged. On March 1, 1944, when the patient was last seen, she had no complaints.

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Department of Statistics

CESAREAN SECTION AT THE BRONX HOSPITAL*

(An Analysis of 494 Operations in 20,763 Deliveries)

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THE report of the Committee on Maternal Mortality¹ which was presented at the Academy of Medicine some years ago, cited numerous instances of cesarean operations which were done by surgeons, dermatologists, nose and throat specialists, and orthopedists. The incidence of the operation was high and the mortality was great. Some time later, from the Hospital Information Bureau,² figures were obtained from five standard and well-known hospitals where the incidence of the cesarean operation varied from one in eleven to one in twenty-four.

Because of the high incidence of the operation and the high mortality, a method was initiated at The Bronx Hospital in an attempt to keep down the number of the cesarean operations. Of course, it was realized that in the case of the private patient, her physician might resort to any procedure that he wished; nevertheless, it was felt that the hospital where the patient was treated has certain responsibilities in regard to the operations performed and must exercise a certain degree of supervision.

The practice then was instituted that the cesarean operation could only be done by the attending and associate obstetricians and gynecologists, and a few other men who were approved by the medical board. Except in the case where the operation was done by the attending physicians, consent had to be obtained before the performance of the section. This approval implied consultation which did not need to be direct. In addition, in cases of cephalopelvic disproportion and contracted pelvis, an x-ray examination was required before the operation. It is needless to say, that in the face of an emergency, such as, hemorrhage from placenta previa, or premature separation of the placenta, telephone permission could be granted.

With these considerations in mind, we have analyzed the figures for the past 10½ years, namely from July, 1932, through December, 1942, at the Bronx Hospital. There were 494 cesarean operations among 20,763 cases. This represents an incidence of one in forty-two or 2.4 per cent. Four hundred and twenty operations were done among 14,977 private patients, or an incidence of one in thirty-six, while on the ward service, there were 74 operations in 5,786 cases, an incidence of one in seventy-eight. This is shown in Table I.

*Read in part, by invitation, at The Bronx Gynecological and Obstetrical Society in May, 1943. Presented at the Section of Obstetrics, New York Academy of Medicine, December 28, 1943.

TABLE I. INCIDENCE

| | NO. OF DELIVERIES | NO. OF CESAREANS | INCIDENCE—1 IN |
|---------|-------------------|------------------|----------------|
| Total | 20,763 | 494 | 42 |
| Private | 14,977 | 420 | 36 |
| Ward | 5,776 | 74 | 78 |

The type of operations are shown in Table II.

TABLE II. TYPE OF OPERATION

| TYPE | TOTAL |
|---------------------|-------|
| Classical | 255 |
| Two flap | 215 |
| Latzko | 13 |
| Waters | 1 |
| Porro | 9 |
| Abdominal pregnancy | 1 |

It is to be noted that in more than half of the cases the classical type of operation was done.

An analysis of the indications for which the cesarean operation was performed is of interest. This is shown in Table III.

TABLE III. INDICATIONS

| INDICATION | NO. OF CASES |
|---------------------------------|--------------|
| Contracted pelvis | 163 |
| Cephalopelvic disproportion | 93 |
| Previous section | 89 |
| Placenta previa | 67 |
| Premature separation | 29 |
| Malpresentation | 8 |
| Cardiac, elective | 5 |
| Toxemias | 7 |
| Stenosis of the vagina | 2 |
| Previous gynecologic operations | 6 |
| Fibroids complicating pregnancy | 9 |
| Postmaturity | 1 |
| Abdominal pregnancy | 1 |
| Fetal distress | 3 |
| Elderly primigravidas | 11 |

It is seen from this Table that in 256 cases, or more than half, the operation was resorted to because of a large baby or small pelvis. It will also be noted that in almost 20 per cent of the patients, the operation was performed because of the previous cesarean. A certain number of these were cases of contracted pelvis or cephalopelvic disproportion, but some represent instances where the original operation had been performed for incidents of pregnancy or accidents of labor. In this connection, reference might be made to recent articles which emphasize the fact that a vaginal delivery may be achieved in cases where the cesarean operation had been resorted to in a preceding pregnancy. In McLane's³ figures from the Johns Hopkins Hospital and those of Kuder⁴ from the New York Lying-in Hospital, more than one-third of the former cesarean cases were delivered per vaginam. Interestingly enough, too, from these articles it is seen that the babies born by the vaginal route were occa-

sionally larger than those born by the cesarean operation, even in cases of contracted pelvis. In addition, there were many cases where evidence indicated that healing had occurred by secondary intention in the course of the previous cesarean section. These studies would indicate that the fact that a cesarean had been performed at one time does not preclude the possibility of a vaginal delivery in a subsequent pregnancy, but the fear of a rupture of the uterus must be kept constantly in mind, and the patients watched with utmost care during their pregnancy and labor.

During the period under discussion, there were 17 deaths among the cesarean cases. This represents a mortality of 3.2 per cent. For the same period under consideration there were 45 obstetric deaths among the 20,763 patients. It can thus be readily seen that more than one-third (i.e. 38 per cent) of the maternal deaths was in cases where the cesarean operation was performed.

An analysis of these deaths (Table IV) shows that ten were among the classical and five among the two flap type.

TABLE IV. MORTALITY

| HOSP. NO. | GRAVIDA | TYPE OF SECTION | INDICATION FOR SECTION | CAUSE OF DEATH |
|-----------|---------|-----------------|----------------------------------|---------------------|
| 35052 | 1 | Classical | Central placenta previa | ? Peritonitis |
| 42845 | 1 | Classical | Funnel pelvis | Peritonitis |
| 61835 | 1 | Classical | Chronic nephritis | Postoperative shock |
| 67950 | 1 | Classical | Cervical malformation | ? Peritonitis |
| 67639 | 1 | Classical | Placenta previa | Peritonitis |
| 75232 | 1 | Classical | Rheumatic heart disease | Cardiac failure |
| 80068 | 1 | Classical | Rheumatic heart disease | Cardiac failure |
| 126307 | 1 | Classical | Cardiac | Pneumonia |
| 138918 | 1 | Classical | Contracted pelvis | ? Peritonitis |
| 117256 | 1 | Classical | Fibroid in lower canal | ? Peritonitis |
| 434145 | 1 | Two flap | Contracted pelvis | Strep. sepsis |
| 47503 | 1 | Two flap | Flat pelvis | Pneumonia |
| 124419 | 1 | Two flap | Elderly primiparas | Shock and collapse |
| 109700 | 1 | Two flap | Contracted pelvis | Peritonitis |
| 124867 | 11 | Two flap | Previous section for flat pelvis | Pulmonary embolism |
| 40100 | 1 | Porro | Central placenta previa | Peritonitis |
| 44529 | 1 | Porro | Intrapartum sepsis | Peritonitis |

Nine patients died of peritonitis and one of sepsis. That is, more than one-half of the deaths were due to infection.

It is interesting here to consider the mortality of the babies. Among the newborn infants, the death rate was 36 in 496 children (two sets of twins), or 8 per cent. Among these there were 16 cases of "ablatio" and 16 premature infants where the operation was done for placenta previa. In both of these indications, the fetus was already dead when the section was done.

As some basis for comparison, the report of DeNormandie² is of value. He gives an analysis of probably the greatest number of cesarean sections that have been collected and reported at one time. He reports on 11,030 cesarean sections in 333,731 deliveries; an incidence of 3.3 per cent. The low cervical operation was done in 53 per cent of the cases while the classical type was done in 42 per cent. Previous section as an indication was present in 29 per cent of the cases. The maternal mortality was 2.5 per cent with sepsis as the cause of death in 39 per cent. The fetal mortality was 9 per cent.

Summary

The cesarean operation is not to be regarded as a panacea for all types of labor and while the operation itself may be simple, it has a real mortality both for the baby and the mother. These must be considered before subjecting any woman to such form of interference.

Conclusion

The striking features of this report from The Bronx Hospital are first, the high maternal and fetal mortality, and secondly, the low incidence of the operation. We feel that the incidence of cesarean sections can still further be reduced. In the case of the elderly primigravida, there should be another indication other than age alone, that is, size of baby, the presentation and the type of pelvis should enter into the consideration.⁶ Also, in the cases of former cesarean sections, the obstetrician may have the courage to permit vaginal delivery, where the operation had been done for a complication of pregnancy, or an accident of labor, or even in some cases of contracted pelvis.

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121 EAST SIXTIETH STREET

1840 GRAND CONCOURSE

1229 CLAY AVENUE

MATERNAL AND INFANT MORTALITY RATES IN 1943

State of Alabama Maternity Clinic Rates, Compared With State Rates as a Whole

WILLIAM A. CUNNINGHAM, M.D., MONTGOMERY, ALA.

(From the Department of Maternal Health, Department of Public Health)

| | STATE | WHITE | COLORED |
|----------------------------|--------|--------|---------|
| Total births | 75,563 | 48,542 | 27,021 |
| Stillbirths | 2,278 | 1,140 | 1,138 |
| Total live births | 73,285 | 47,402 | 25,883 |
| <i>Clinic Patients:</i> | | | |
| Total births | 8,764 | 1,121 | 7,643 |
| Stillbirths | 223 | 19 | 204 |
| Total live births | 8,541 | 1,102 | 7,439 |
| <i>Nonclinic Patients:</i> | | | |
| Total births | 66,799 | 47,421 | 19,378 |
| Stillbirths | 2,055 | 1,121 | 934 |
| Total live births | 64,744 | 46,300 | 18,444 |

12 per cent of all maternity patients attended state clinics.

2.3 per cent of white maternity patients attended state clinics (1 out of 40).

28 per cent of colored maternity patients attended state clinics (3 out of 10).

Seven times as many colored as white attended clinics.

Approximately 70 per cent of the colored are delivered by midwives; in Montgomery County—95 per cent.

Approximately 90 per cent of the colored are delivered at home.

In rural Alabama over 80 per cent of the colored are delivered by midwives and 97 per cent at home.

STATE AS A WHOLE (NUMBER AND RATE)

| | TOTAL | | WHITE | | COLORED | |
|--|-------|------|-------|------|---------|------|
| | NO. | RATE | NO. | RATE | NO. | RATE |
| Maternal mortality (per 10,000 total births) | 228 | 30.2 | 111 | 22.9 | 117 | 43.3 |
| Neonatal mortality (per 1,000 live births) | 1,917 | 26.2 | 1,114 | 23.5 | 803 | 31.0 |
| Stillbirths (per 1,000 total births) | 2,278 | 30.1 | 1,140 | 23.5 | 1,138 | 42.1 |

COMPARISON OF THE RATES OF NONCLINIC WITH CLINIC PATIENTS, STATE OF ALABAMA AS A WHOLE

| | NONCLINIC | | | CLINIC | | |
|--------------------|-----------|-------|---------|--------|-------|---------|
| | TOTAL | WHITE | COLORED | TOTAL | WHITE | COLORED |
| Maternal mortality | 31.3 | 22.8 | 52.1 | 21.7 | 26.8 | 20.9* |
| Neonatal mortality | 27.6 | 23.8 | 31.8 | 15.0 | 10.9* | 15.0* |
| Stillbirths | 30.8 | 23.6 | 48.2 | 25.4 | 16.9* | 26.7 |

*Specially outstanding.

Of special import are the following deductions:

1. Total clinic rates are greatly lower than nonclinic rates in all three categories: a 31 per cent reduction in maternal mortality, a 36 per cent reduction in neonatal mortality, and an 18 per cent reduction in stillbirths.

2. In nonclinic patients, the colored rates are double the white rates in maternal mortality and stillbirths, and 34 per cent higher in neonatal mortality.

3. The colored clinic rates are below the total state rates in all three categories: in maternal mortality by 30 per cent, in neonatal mortality by 40 per cent, and stillbirths by 12 per cent.

4. If we take the two opposite extremes economically and educationally, namely the white private (nonclinic) patient and the colored clinic patient, it is rather startling to find that the colored rate is lower than the white in maternal mortality by 9 per cent and neonatal mortality by 35 per cent; but higher in stillbirths by 13 per cent, probably in the main because of the prevalence of syphilis in the colored.

5. The colored clinic rates are tremendously below the colored nonclinic rates; in maternal mortality by 60 per cent, in neonatal mortality by 51 per cent and in stillbirths by 45 per cent.

6. The white clinic rates are lower than the white nonclinic rates terrifically in neonatal mortality—54 per cent and in stillbirths—28 per cent, apparently because of better supervision of nutrition and syphilis in the mother and infant. Private physicians do not all take serologic tests for syphilis. The maternal mortality rate for white clinic patients however was above that for nonclinic patients by 17 per cent which is understandable since more of them are delivered by midwives, and more home deliveries occur. The economic, educational and social status of the clinic patient is definitely lower than the private patient, and her delivery and aftercare is poorer.

7. As a continuance of Item 2, if we compare colored rates with white in clinic patients, we find the colored rate lower by 22 per cent in maternal mortality, but higher by 43 per cent in neonatal mortality and 58 per cent in stillbirths. The first finding is difficult to explain but the answer to the latter two probably lies again in the prevalence of syphilis in the colored, plus their background of economic and educational inferiority.

8. Although in 1943, there were slightly better than five white births in Alabama to every three colored births, the absolute number of maternal deaths and stillbirths were almost identical. In neonatal mortality however, the colored were almost 30 per cent lower which is more in proportion.

MATERNAL MORTALITY, INFANT MORTALITY, NEONATAL MORTALITY AND STILLBIRTH RATES

STATE OF ALABAMA—1938, 1940, 1942 AND 1943

| | TOTAL | | | | WHITE | | | | COLORED | | | |
|---|-------|------|------|------|-------|------|------|------|---------|------|------|------|
| | 1938 | 1940 | 1942 | 1943 | 1938 | 1940 | 1942 | 1943 | 1938 | 1940 | 1942 | 1943 |
| Maternal mortality (per 10,000 total births) | 63.0 | 58.8 | 38.6 | 30.2 | 51.1 | 39.7 | 27.4 | 22.9 | 82.9 | 89.0 | 57.3 | 43.3 |
| Neonatal mortality (under 1 month) (per 1,000 live births) | 36.3 | 38.3 | 30.5 | 26.2 | 32.0 | 33.0 | 26.6 | 23.5 | 44.2 | 47.3 | 37.4 | 31.0 |
| Infant mortality (under 1 year) (per 1,000 live births) | 60.6 | 61.3 | 50.1 | -- | 53.5 | 51.1 | 40.7 | -- | 72.5 | 77.9 | 66.4 | -- |
| Stillbirths (per 1,000 total births) | 40.2 | 38.4 | 31.9 | 30.1 | 28.3 | 28.0 | -- | 23.5 | 59.5 | 54.8 | -- | 42.1 |

COMPARATIVE STATISTICS—1940 TO 1943

| TOTAL RATES | MATERNAL MORTALITY | NEONATAL MORTALITY | STILLBIRTHS |
|-------------------|--------------------|--------------------|-------------|
| 1940 | 58.8 | 38.3 | 38.4 |
| 1941 | 49.6 | 36.0 | 37.6 |
| 1942 | 38.6 | 30.5 | 31.9 |
| 1943 | 30.2 | 26.2 | 30.1 |
| Overall Reduction | 49% | 32% | 22% |

1943 STATISTICS

12 per cent of all maternity patients attended state clinics; seven times as many colored as white attended clinics.

There were 75,563 total births: white—48,542, and colored—27,021. Live births—73,285: white—47,402, colored—25,883.

There were 2,278 stillbirths: white—1,140, and colored—1,138.

Patients attending maternity clinics—8,764 total births: white—1,121, and colored—7,643.

Correspondence

To the Editor:

The long, bloody, tragic history of accouchement forcé has been noted in many obstetric chronicles. More urgently, the nightmarish effects of the procedure are sharply etched in the minds of a still living generation of obstetricians.

A happily forgotten method, it was disinterred in 1929 by Delmas, whose sole modification resided in the fact that he carried it out under spinal anesthesia. As might have been anticipated, Delmas' idea fell rapidly into disrepute and perhaps the obstetric world breathed a great sigh of relief.

Within the last year or two manual dilatation of the cervix under spinal anesthesia (as an elective measure to terminate pregnancy before the onset of labor) was again revived and championed by two surgeons, Koster and Perrotta. (See the 1943 Yearbook of Obstetrics and Gynecology.) It was my good fortune to have had a long conference with Koster concerning the technique he employed. After discussing the method with him, I obtained permission to employ it on the service at Harlem Hospital in a series of cases.

Our experience finds us in wide disagreement with Rosenfeld who reports five cases in the May issue of the JOURNAL: Vol. 47, No. 5, pp. 699-702. We are more interested in at least one statement made by Rosenfeld than we are in the five very interesting cases he presents. On page 701 he states, "It can be demonstrated pharmacologically and certainly clinically that spinal anesthesia relaxes the cervical muscles so that the cervix can be easily dilated, and at the same time, it causes contraction of the corporeal muscles."

Before advancing to pharmacologic or clinical demonstration perhaps an anatomical and histological study would be of value. For example: what are the "cervical muscles"? How do they differ histologically from the corporeal muscle? Are there muscles in the cervix at term or are there merely some muscle fibers? What is the innervation of the cervix? Is there a nerve distribution so arranged that the spinal anesthesia produces the almost incredible effect attributed to it? Why should the muscle fibers in one portion of an organ relax when the tonus of fibers in another portion of the same organ increases? What is the mechanism? Is it possible to efface the cervix manually? These are some of the questions which arise out of theoretic consideration of the method.

From actual utilization of the technique as described by Koster and Perrotta, we have drawn certain conclusions which we have listed dogmatically below. We departed from their technique in that we used 100 mg. of procaine rather than 150 mg. We reduced the dosage because they informed us that they used the larger dosage only out of habit.

From the experiences of Dr. Kassebohm and myself, we feel that the following conclusions are fairly drawn: 1. There is no change in the consistency of the cervix following spinal anesthesia. 2. Where the cervix is completely effaced, there is no change in the consistency of the tissues which bound the os. 3. There is no notable difference in manual dilatation relating to the type of anesthesia. 4. Manual dilatation may be performed under general inhalation anesthesia, pre-sacral block, caudal analgesia, intravenous anesthesia or spinal anesthesia. 5. Rapidity of dilatation results from the dexterity of the operator and the fortuitous elasticity of the cervix; the type of anesthesia has no bearing. 6. With no twinge of conscience and no apology, a too often unremembered cliché must be stated, i.e., manual dilatation means manual laceration.

In such unusual instances as reported by Rosenfeld, rapid delivery by accouchement forcé may be indicated. Rosenfeld warns of the dangers of the procedure and calls for expert attendants. Unfortunately the method may, and to our knowledge, already has reached hands which cannot be so classified. Further it has been used, not in the rare emergency but as an elective procedure to guarantee painless labor. There is no point in listing the dangers attached to such foolhardiness.

Accouchement forcé has too often been life giving and death dealing. Spinal anesthesia has not altered its basic aphysiologic character. It were better that it again be interred and this time its grave firmly and forever sealed lest it again force the opening of graves for mothers. Obstetric art and obstetric conscience will grow without it and the latter will rest more easily.

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NEW YORK, N. Y.
MAY 31, 1944

To the Editor:

For a number of years I have been impressed by the lack of an adequate descriptive term of the patient who calls on the members of our specialty to discover why she has not borne children. The terms "sterile," "barren," and "childless" have been neither scientifically accurate nor esthetically acceptable. "Sterile" and "barren" convey implications which, conventionally and historically, are uncomplimentary and condemnatory. "Childless" is equally indefinite.

I am sure that other members of the specialty have experienced the same reaction with regard to these terms, because I have talked with many of them. The result is that I have been trying to find a term that described the patient who has not borne children, although exposed to normal marital relations over a reasonable period of time, and who now seeks to find the reason.

I have enlisted the aid of Professor (Dean) John C. Bailey, Jr., of Davidson College, a man of no little renown in the matter of language research, and he has come forward with what seems to me to be a practical answer. He suggests the noun "agennesis" and "agennetic" as the adjective. According to this authority, all the necessary descriptive needs are contained in these two words.

He calls attention to the following two points: first, both of these words are spelled with two n's; second, the noun "agennesis" is accented on next to the last syllable, and the "e" in that syllable is long, as in "we."

I would, therefore, request space in your JOURNAL for this proposed addition to our gynecologic and obstetric nomenclature, and thereby at least bring the matter up for discussion, and perhaps a still better term may be discovered.

OREN MOORE, M.D.

CHARLOTTE, N. C.
APRIL 20, 1944.

Department of Reviews and Abstracts

Selected Abstracts

Malignancies

Ferris, D. O., and Dockerty, M. B.: Adenocarcinoma of the Body of the Uterus Arising From a Benign Endometrial Polyp: Report of Case, Proc. Staff Meet. Mayo Clinic 19: 133, 1944.

The authors present a case report dealing with an endometrial polyp which became the source of an adenocarcinoma of the body of the uterus. The authors point out that such a transformation is extremely rare and must fulfill certain criteria such as:

1. The carcinoma must be confined to one portion of the polyp.
2. The base of the polyp must be benign.
3. The surface of the endometrium around the base of the polyp must show no malignant change.

Their case report fulfills the recognized requirements.

JAMES P. MARR

Morton, Daniel G.: Carcinoma of the Uterine Cervix: Prognosis and Treatment, West. J. Surg. 52: 1, 1944.

Radiation holds first place in the treatment of cervical carcinoma; however, the author believes that surgery still has a limited field of usefulness. Until 1931, the cases at the University of California were treated by radium in the smaller dosage of that day and only occasionally was x-irradiation used for metastasis or extension. Now the x-irradiation is carried up to 3,000 or even 4,000 roentgens. It is believed to be an essential and indispensable part of the therapy not only for its effect upon the primary lesion and the area of primary spread. Roentgen irradiation is not a benign procedure, however. It precipitated death in 18 of the 374 cases here reported. Vascular changes, fibrosis, bone necrosis, and ischemic ulceration of the bowels are a few of the complications encountered.

The treatment plan used by this author is described. Four thousand, five hundred milligram-hours of radium are given in three doses at weekly intervals; 3,000 milligram-hours in the cervicouterine canal and 1,500 milligram-hours in a plaque across the cervix. The author has a mild preference for x-irradiation completed about three weeks before the use of radium, but he has used them concurrently and even reversed the sequence without a great difference in results. The advantage of x-irradiation first is that a large, fungating mass can be reduced; and perhaps more important the sloughing cervical mass which is always septic can be cleaned up. Reirradiation is not recommended, the incidence of slough is high and the results are not improved. All therapeutic effect is attained in the initial course of treatment.

Comment is made upon 100 Wertheim operations performed in this clinic for early Schmitz Stage I and II carcinoma. Prognosis in carcinoma of cervix is reasonably good, a hopeless attitude is not justified. The clinical stage of the disease and its immediate response to treatment are the best guides to prognosis.

WILLIAM BICKERS

Cesarean Section

Lull, Clifford B., and Ullery, John C.: Cesarean Section Under Continuous Caudal Analgesia, *J. A. M. A.* 142: 90, 1944.

The authors report their observations on 50 cases operated upon at different institutions. Contraindications to the use of caudal anesthesia are enumerated, and the mental preparation of the patient to the procedure is stressed. It has not been used in cases of placenta previa. Barbiturates are given the night before and one hour before the operation. Fifty mg. of ephedrine hydrochloride are given to the patient if the blood pressure is below 140 mm. systolic. In hypertension cases, it is withheld unless the blood pressure falls to 100 mm. systolic. The technique of administration is outlined. Metycaine was used in all cases. None of the babies needed resuscitation. The average estimated blood loss was 100 c.c., the patients are greatly benefited by the administration of morphine and scopolamine immediately after abdominal section or vaginal delivery.

WILLIAM BERMAN

Zecena, Arturo: A Manipulation to Extract the Fetal Head in Low Cesarean Section, *Obst. y ginec. Latino-Americanas* 1: 356-358, 1943.

The author comments that manual extraction of the head during cesarean section has been mentioned by other authors, but without details. The following procedure has been used successfully in 15 successive cases.

The operator, standing to the left of the patient and facing her feet, carries out the manipulation with the right hand. With a movement of forced pronation, he turns the palm of his hand so that it is facing the face of the patient. He introduces the fingers with the exception of the thumb between the left border of the uterine incision and the fetal head. Taking a step forward, in order to increase the extension of the arm, by movements of flexion of the fingers, he turns the fetal head until it lies on the palm of his hand. If necessary, an assistant exerts pressure deeper in the uterus at the proper moment, to aid in the expulsion.

This manipulation is easily carried out and does not present the difficulties of other procedures (increase of diameter of the fetal head, injury, infection, etc.) and, hence, is recommended by the author.

J. P. GREENHILL

Perez, M. L., and Echevarria, R.: Intraperitoneal Sulfanilamide Treatment in Cesarean Section, of Infected Cases, *An. Inst. de Mat. y Assist. Soc.* 4: 9-15, 1942.

The authors have used sulfanilamide intraperitoneally in cases of the low cervical cesarean section where contamination of the peritoneal cavity would have followed operation. The amounts used were large, never less than 6 to 8 mg. and this level was maintained for 3 or 4 days. In 11 previously reported cases, there was no peritoneal infection but there was one death. This was proved to be due to sulfanilamide poisoning and followed the instillation of 5 Gm. of sulfanilamide intraperitoneally.

J. P. GREENHILL

Endocrinology

Borras, P. E.: Possible Hormonal Effect of the Endometrium on Ovary of Hysterectomized Animals, *An. Catedra de clin. ginec.* 2: 104-107, 1943.

Such an effect is suggested by the author on the basis of experiments in rabbits which received injections of the lipoid fraction of extract of endometrium. The experiments showed that uterine extracts exert a demonstrable action on the ovary, which corroborates the uteroovarian hormonal correlation. They suggest clinical trial of uterine extracts, so far not investigated, in the treatment of glandular insufficiency in women.

Although these experimental results have been duplicated by other workers, the author advances a word of caution regarding interpretation of these results. He points out that extracts of the endometrium contain a considerable quantity of estrogenic substances and that the results obtained may be nothing more than the effect of these substances, rather than a supposed endocrine capacity of the endometrium. Numerous experiments to test this hypothesis have been devised and partially accomplished, and none of the evidence so far accumulated tends to indicate that the results are due to estrogenic substances. Hence, the author believes that endometrial extracts act in a very specific way, without any relation to their possible estrogenic effect.

J. P. GREENHILL

Belizan, L. A.: Treatment of Certain Female Sexual Disorders by Transplantation of the Pituitary, *An. Catedra de clin. ginec.* 2: 213-233, 1943.

The author reports a second series of thirteen cases in which the technique of hypophyseal implantation was modified slightly from that generally used, and which he had employed in an earlier series of eleven cases.

Patients were chosen with a general or ovarian disturbance which could be regarded as secondary to a primary pituitary deficiency. Most of the patients had not responded satisfactorily to other types of treatment. Only one implantation was made, with no other treatment to supplement it, in order to determine categorically whether this procedure is efficacious and if so, to determine the duration of its effect.

In some patients, an effect was produced which lasted approximately four months and in others, there was no effect. In the first series, the most definite effect seemed to be in connection with libido and the orgasm, but these were not improved in any patient in the second series. On the other hand, there were many menstrual changes; oligomenorrhea and hypomenorrhea were benefited especially, although the benefit was distinctly temporary.

J. P. GREENHILL

Caso, F. C.: Endocrinology and Stomatologic Practice, *Gac. méd. de México* 73: 409-415, 1943.

In hyperthyroidism, sometimes several teeth are present at birth; caries are frequent from lack of calcium; the superior maxillary bones are fragile; and there is increased salivation. In hypothyroidism, characteristic changes include: delayed dental development, large central incisors, small lateral incisors, overlying teeth, congenital malformations of the mouth and teeth, malocclusion, chronic infection of the tonsils and chest, enamel and dentine abnormally soft, radicular reabsorption, decreased density of the crowns, decalcification of the bones of the wrist and of the superior maxilla, hypertrophic tonsils and dry mouth.

In pituitary hyperfunction, there may be early eruption, large teeth of square type, wide superior incisors widely spaced, with errors of alinement, teeth resistant to caries, marked mandibular hypertrophy. With hypopituitarism, common changes are late eruption, small mandible (overbite), small, infantile teeth, flattened canines, rapid caries, crowded teeth, teeth of bluish tint, possible pyorrhea.

In hypertrophy of the thymus, there are delayed eruption, small upper maxilla, large central incisors, flattened lateral incisors, poor enamel, extensive caries, congenital malformations of the mouth and upper and lower jaws, hypertrophied tonsils and glands, and pyorrhea. With diabetes, there is early eruption, extensive caries, granulomas, inflammation of the edges of the tongue, abscesses and fissures of the tongue, gingivitis and ulcerations, pyorrhea, stomatitis, dry mouth, increased cholesterol in the saliva, acrid and metallic breath.

In hyperadrenalism, early eruption and very large canines are noted. With hypoadrenalism, the teeth are yellowed, and there are many dark spots on the mucous membrane. With hypergonadism, frequent caries and early loss of the teeth are characteristic. In hypogonadism, the lateral incisors and canines are flattened, and this condition may have a causal relationship to pyorrhea. In pregnancy, there are caries through loss of calcium, as well as change of color of the teeth, hypertrophy of the gums, gingivitis and paresthesia of the oral mucosa.

In hyperparathyroidism, changes include decalcification of dentine, with frequent caries and difficult preparation of cavities for fillings, radicular infection, and mandibular giant-cell tumors. In hypoparathyroidism, there are atrophic teeth in cradle form, defective enamel, lateral erosion of teeth, horizontal cracks and furrows of the enamel, and a possible connection with pyorrhea.

The author concludes that the endocrinopathies have marked repercussions in the mouth, and once these are recognized, the dental surgeon can collaborate with the physician in treatment. He points out that pyorrhea is not a pathologic entity, but a syndrome related to endocrine dysfunction; thus the infectious theory is superseded. The microorganisms (nonspecific in this case) develop at a site of least resistance, but the cause of dental decalcification should be sought in the body, and especially in the glands of internal secretion.

J. P. GREENHILL

Bishop, P. M. F., and Folley, S. J.: *Implantation of Testosterone in Cast Pellets*, *Lancet* 246: 434, 1944.

The authors, for over a year, have been studying, with reference to ghost formation, the absorption of cast and compressed pellets of steroid hormones implanted for clinical purposes in human subjects.

The writers implanted 100 mg. pellets of testosterone into male subjects. These were removed, reweighed and quantitatively extracted with ether. No evidence of ghost formation was demonstrable in the interior of the pellets. There was also a satisfactory agreement between the experimental determinations and theoretical curve indicating that the *in vivo* absorption rate of a cast pellet at any instant is proportional to its surface area, allowing for the conclusion that encapsulation, which was observed in most cases, has no progressive retarding effect.

The initial absorption rate of the authors' implanted pellets was approximately 1.1 mg. per day, but by 50 days this had been reduced by a third. Cast pellets were absorbed faster (12 per cent greater) than the compressed pellets. This phenomenon is explained primarily by the greater surface area of the cast pellets. The twenty determinations of the authors illustrate most succinctly their conclusions.

C. E. FOLLOME

Extrauterine Pregnancy

De Queiroz, Alicio Peltrier: Advanced Ectopic Pregnancy, *An. brasil. de ginec.* 7: 193-202, 1942.

According to the author, advanced ectopic pregnancy is one that has progressed beyond the fourth month. Some of these cases may progress to term and a live fetus be extracted. The chances of survival are, however, very slim for most of these fetuses present deformities incompatible with life. In other cases, whether or not the pregnancy has reached term, the fetus dies after "false labor," and is retained as a fetal cyst. The contents of an aseptic fetal cyst may undergo various changes like mummification, skeletization, saponification, calcification, etc. The ovum may, however, become infected, causing suppuration with all its sequelae, including peritonitis and death. On the other hand, in some cases, this suppuration of the cyst may lead to a spontaneous cure, in that the cyst perforates into the bladder, rectum or through the abdominal wall.

The first of the two cases dealt with in the present communication was that of a woman, aged 34, para vi, who became pregnant two years previously, carried the pregnancy to the eighth month, and was found on operation, at the twenty-fourth month, to have an intraligamentary fetal cyst. Because of technical reasons, a supravaginal hysterectomy with removal of both adnexa was performed. The second case was that of a woman, aged 34, in whom pregnancy likewise progressed until the eighth month, the operation being performed at the twelfth month. This consisted of sectioning and emptying the cyst with partial removal, after separation of adhesions which fixed the cyst to the mesosigmoid and to the Douglas pouch. Both patients showed uneventful recoveries.

J. P. GREENHILL

King, Samuel L.: Coexisting Intrauterine and Extrauterine Pregnancies, New England J. Med. 229: 965, 1943.

The author presents a case report dealing with coexistence of intrauterine and extrauterine pregnancy.

No extrauterine mass was palpable preoperatively, but signs and symptoms of intraperitoneal hemorrhage and a suspected ectopic gestation led the surgeon to perform a laparotomy. A bilateral salpingectomy and appendectomy were performed. The intrauterine pregnancy continued to near term.

JAMES P. MARR

Gynecology

Araya, R.: Fundamental Concepts of Ovarian Histophysiology, *An. Catedra de clin. ginec.* 2: 30-68, 1943.

The author presents a histologic study of 50 ovaries removed from patients aged 20 to 40, correlated with the menstrual cycle. A previous study had shown no correlation between ovulation and menstruation, i.e., ovulation was demonstrated to occur at any time during the menstrual cycle.

These careful microscopic studies of all elements of the ovary confirm the concept concerning the development of hormonal function of the ovary. Development of the hormonal functions is intimately related, on the other hand, to the activities of the entire body, especially to those of other endocrine glands, particularly the pituitary.

Various organs of the body participate in the menstrual process, transporting by way of the circulating blood elements indispensable to regular development of its essential functions, related to reproduction and preservation of the species. The

anterior hypophysis is especially important, which by means of a follicle-stimulating hormone (gametotropic) and a luteinizing fraction (hormonotropic) stimulates the hormonal activities of the ovary, which, by means of its estrogenic-folliculin and luteinizing-progesterone secretions causes changes in the endometrium which lead to menstrual loss when the ovum has not been fertilized. Participation of the entire body and of particular organs in the menstrual process is evidenced by trophic and functional disturbances of the genital apparatus, produced in the course of illness. Among the former are atrophy and hypertrophy of the genitalia; and the latter are manifested by anomalies of menstruation.

The literature abounds in examples, outlining effects of chronic diseases, intoxications, blood diseases, and of diseases of various organs, such as the heart, kidneys and of endocrine diseases, affecting the pancreas, thyroid, adrenals, and of vasomotor disturbances, or diseases of the autonomic, or central nervous systems.

The author includes a graphic presentation of four successive menstrual cycles, in which the ovum was formed in only three, and these at different periods of the cycle, notwithstanding the fact that the cycle was in all instances completely normal. This is because the menstrual process is the result of integral activities of the ovary, within which a prominent role is played by the development of numerous primordial follicles which tend toward atresia, and among which only one or two may be transformed into Graafian follicles, which in turn may or may not develop into a mature ovum.

J. P. GREENHILL

Ahumada, J. C., Chevalier, R. M., and Sammartino, R.: *Actinomycosis of the Ovary*, *Bol. Soc. de obst. y ginec. de Buenos Aires* 22: 362-370, 1943.

The patient, a single woman, aged 24, first had acute symptoms in the abdomen, localized in the right lower quadrant, which were interpreted as appendicitis. Successive laparotomies marked a serious surgical course which caused her death three years later, despite combined therapy employed to combat the infection.

The infection can reach the genital organs through the ascending, or intracanalicular route; the hematogenous, with metastases; and the entral, that is the rectosigmoid or cecal, favored by scant peristalsis, cecal stagnation and mucous microtrauma. From this site, it spreads by the intraperitoneal route through adhesions, or extraperitoneally through the peritoneum connecting with the ovaries. Actinomycosis of the ovary may be primary, i.e., confined to the genital apparatus; diffuse throughout the whole system (50 per cent); or enclosed (?) actinomycosis, localized in a pre-existing genital cystic lesion.

The lesion consists of hard callus, pierced with numerous cavities filled with pus; this explains the progression and diffusion, and the tendency to extend to the Retzius cavity, the retroperitoneum, the iliac fossae, perineum, or abdominal skin, and even to neighboring organs, the rectum, bladder and vagina.

The symptoms do not form a clinical cavity: the disease may begin with acute abdominal symptoms, in an incipient form, or even without symptoms, until it is diagnosed as a tumor. With progression, there are various types of pain, febrile reactions, symptoms of colitis, with alteration of the sexual cycle only in the final stages. Progression is inter-perred with apparent remissions, purulent fusion and secondary fistula formation, invasive tendency, abscess formation with but slight healing of the cavities, and a tendency to new fistula formation with invasion of the zones mentioned.

Definite diagnosis depends on histologic study and isolation of the organism. The prognosis is extremely serious, with cures reported ranging between 10 and 40 per cent. In the treatment there are three procedures: surgery, roentgen therapy and chemotherapy with iodine and arsenical preparations, and in some instances specific vaccine. Their efficacy is dependent on early diagnosis and limitation of the lesion.

J. P. GREENHILL

De Moraes, A.: War Trauma and the Female Genital Apparatus, *An. brasil de ginec.* 8: 283-294, 1943.

Due to the type of war now being fought, everyone may be injured by air bombardment. The author presents the following outline of the ways in which war trauma may effect the female genital apparatus.

I. By direct action on the genital apparatus

1. In pregnant women
2. In nonpregnant women
 - a. Normal genital tract
 - b. Pathologic genital tract

II. Repercussion on the female genital apparatus and its functions by traumatic agents acting at a distance

1. By physical action (displacements of the body)
2. By action on the vegetative nervous system (emotion)

III. Skeletal lesions with primary and secondary effects on the bones of the pelvis affecting the reproductive process.

J. P. GREENHILL

Chevalier, R. M., and Salaber, J. A.: Chorionepithelioma: Diagnostic and Therapeutic Considerations, *Obst. y ginec. Latino-Americanas* 1: 471-478, 1943.

The authors suggest after a thorough review of the literature, that the diagnosis of chorionepithelioma should be accomplished in three separate steps; clinical, anatomic, and biologic. The clinical symptoms depend on localization, whether or not there is a coexistent normal or pathologic pregnancy, and the presence or absence of metastases. The degree of malignancy also accounts for much variation in symptoms. In intra-cavitary uterine chorionepithelioma, the classic triad of symptoms consists of recurring metrorrhagia, serous discharge from necrosis of the tumor, and fever, indicating infection or thrombosis in an anemic patient, with transparent pallor and ash color, and with albuminuria and cylindruria. Examination reveals a globular uterus, smooth, soft, movable, with a softened cervix. Sometimes the cervical orifice is open, permitting intrauterine palpation. Intramural chorionepithelioma is asymptomatic until it perforates the endometrium or perimetrium. When the lesion is situated in the cervix, the significant finding is repeated metrorrhagia which does not respond to curettage, whose true nature finally is revealed by histologic study or metastases.

The clinical examination is completed with hematologic and radiographic studies, and then histologic study of material from the cervical or intrauterine cavity is made. Interpretation is somewhat difficult, because the elements constituting the tumor are morphologically and biologically identical with cells derived from the trophoblast, giving rise to doubt as to whether they are from a chorionepithelioma, or from ovarian rests. The following are considered as presumptive indications of chorionepithelioma: (1) Marked solid proliferation of the chorial epithelium; (2) existence of changed maternal tissue when deep portions are obtained.

Biochemical investigation yields confirmatory evidence of the presence of chorionepithelioma, which usually is accompanied by excessive gonadotropic hormone, although some negative tests have been reported. The authors believe the value of biologic determinations lies in serial tests and in correlation with clinical and pathologic findings.

The plan of treatment in a patient with chorionepithelioma should be: (1) Complete clinical study; (2) investigation of metastases; (3) surgical treatment by the abdominal route, permitting complete examination of the genital organs, finding the exact situation of the tumor, and, in removing it, reducing uterine trauma to a minimum with ligation of the veins to prevent operative embolism; (4) in ac-

cordance with the extent of the lesion and the patient's age, total hysterectomy, or subtotal, with the possibility of saving the adnexa; (5) roentgen therapy for visceral metastases; (6) vaginal surgery and radium for vaginal metastases.

J. P. GREENHILL

D'Aquila, H. P.: Erythro sedimentation in Complicated Myomas, *An. Catedra de clin. ginec.* 2: 251-258, 1943.

The author discusses this subject with details from nine illustrative cases. She believes that a high sedimentation rate in the presence of uterine fibromyoma (eliminating other causes for this finding) is a definite indication of a complicated lesion, even though gynecologic examination may not reveal any abnormality. Histopathologic study should always be carried out after operation for removal of a myoma accompanied by high sedimentation rate. This will reveal areas of tissue showing necrobiosis, hyaline and mucous degenerations, localized infection, and sometimes sarcomatous and carcinomatous zones. Circulatory changes constitute approximately 30 per cent of the complications in uterine myomas.

J. P. GREENHILL

Lavarello, A. G.: Central Abscess of the Ovary, *An. Catedra de clin. ginec.* 2: 272-288, 1943.

Central abscess of the ovary and abscess of the corpus luteum are, from the anatomopathologic standpoint, two distinct processes. The former, surrounded, that is, within the elements of the organ, causes profound changes both in function and structure; there are progressive stages, from normal tissue to total destruction of the ovary, at whose expense the purulent cavity is formed. In an abscess of the corpus luteum, the process may be called peripheral, and there is not destruction, but alteration, usually of the infiltrative type, of the parts of the ovary adjoining the process.

Most authors regard the pathogenesis of central abscess as of puerperal origin, either post partum or postabortive, and from his observations, the author is inclined to agree.

In regard to classification, the author suggests that, on an anatomopathologic basis, central abscess should be included in chronic interstitial oophoritis, while luteal abscess belongs to the acute types of ovarian inflammation due to peripheral infection.

J. P. GREENHILL

Bates, Robley, Jr., and Rucker, Pierce M.: Tuberculosis of the Vulva, *Virginia M. Monthly* 71: 199, 1944.

Tuberculosis of the vulva is the rarest form of genital tuberculosis. It must be differentiated from esthiomene, tertiary syphilis, granuloma inguinale, and carcinoma. The vulval lesion may be either primary or secondary, the former being rare and difficult to prove conclusively. That it may be acquired by local inoculation at coitus is open to question, but it is true that the disease has been produced in the vagina of guinea pigs after first sensitizing the animals. In the secondary cases, the infection often extends from a neighboring organ such as bladder or rectum, and of course, may result from a descending infection from the vagina or uterus.

Prognosis must be guarded, spontaneous healing sometimes occurs. The treatment is not well established, but cases are cited from the literature treated by excision, radiation, or local application of zinc chloride in alcohol.

The authors report a case of secondary vulval tuberculosis with a history of pulmonary tuberculosis in 1935, a history of rectovaginal fistula in 1932. At the

age of 44, she reported for examination, not for the ulcer on her vulva, but to see if she was pregnant. A photograph of the lesion is shown together with the photomicrograph of the tissue removed for biopsy. The base of the ulcer was granular and bathed with pus, it was acutely tender. The genitals were otherwise negative. The pathologist reported, "nests of epithelioid cells situated just below the epithelium and surrounding giant cells of the tuberculous type." Although acid-fast stains could not be done, the histologic findings were characteristic of tuberculosis.

No treatment was instituted because of the patient's extreme pulmonary involvement. She died a few months after the local lesion was discovered.

WILLIAM BICKERS

Gynecologic Operations

Borras, P. E.: Obstruction of the Bladder Neck in Women, An. Catedra de clin. ginec. 2: 130-156, 1943.

Two cases are reported by the author with discussion of symptoms, endoscopic signs, pathologic anatomy and treatment. The outstanding symptom is painful and difficult urination. Occasionally, there is some hematuria and urinary retention. Following the local symptoms, general disturbances result from lack of rest, distracting pain, inability to work, and increasing nervousness, which is exaggerated with the failure of all medical treatment. The cystoscopic picture is characterized by thickness of the vesical columns and cells, and sometimes by true diverticuli, which reflect the pressure to which the bladder musculature has been subjected because of the obstruction at the outlet due to rigidity of the sphincter. The muscular coat of the sphincter, histologically, shows, marked hypertrophy and hyperplasia of the fibers, changing their disposition into a picture resembling uterine myoma. Within the muscular tissue, infiltration of inflammatory elements may be found, and always a sclerotic process which leads toward fibrous transformation of these elements of the bladder neck.

Once the diagnosis of disease of the bladder neck has been made, there is only one treatment and that is surgical. It is necessary to open the bladder neck itself, and three routes may be utilized, perineal, endourethral or vaginal, and transurethral. The sclerotic portion of the bladder neck is destroyed through a resectoscope, preferably, the MacCarthy instrument, because it allows vision of the surgical field, and extensive areas of tissue can be resected rapidly, because of the variation in form and size of the electrodes. The two patients reported were operated by the transvesical route, because a MacCarthy resectoscope was not available at the time, and the transurethral route promised to be difficult because the bladder in both instances could stand little distention. Marion prefers the transvesical route in all cases because it allows complete and radical operation without increasing the risks, and because it permits exact calculation of the zone to be extirpated, and even allows complete removal of the bladder neck. The author, however, notwithstanding the good results in his two cases with this method, believes that, generally, the transurethral approach is the one of choice.

J. P. GREENHILL

Borras, P. E.: Morbidity and Mortality in Surgical Treatment of Uterine Tumors, An. Catedra de clin. ginec. 2: 90-96, 1943.

The author presents a statistical study of 1,240 cases representing a 30-year experience on two surgical services. In the majority of instances (968), the tumors were fibromyomas; in only 22 cases was cancer present with the fibromas. The predominant symptom was menorrhagia or metrorrhagia in 687 cases (54.83 percent). In 663 instances, another operation, such as appendectomy, salpingectomy, etc., was performed concomitantly.

Postoperative complications occurred in 346 of the 1,240 cases, the majority caused by pulmonary processes (38.72 per cent). In order of frequency were the following: phlebitis, paralytic ileus, parotitis, cystitis, surgical shock and fever of undetermined cause. Cardiovascular complications included collapse, peripheral failure and cardiac insufficiency.

Of 139 patients who had total hysterectomies, 108 had some postoperative disturbance. Among 769 cases in which subtotal hysterectomy was performed, complications occurred in only 95. In reviewing the record of complications in recent years, it is obvious that newer methods of preparing patients for surgery and recent pathogenic concepts of certain complications facilitate prevention and treatment of all postoperative difficulties. This study indicates that the index of mortality has decreased constantly and now is not more than 2 to 3 per cent.

In the statistics for the 30-year period, the mortality rate for surgery of the uterine muscle was 7.18 per cent. In contrast to this, in the last five years, it was 1.8 per cent. Nevertheless, it is only fair to recall that formerly patients would submit to operation only in advanced stages, whereas now surgery is carried out much earlier in many cases. Of 1,240 patients in the entire series, 89 died. The greatest number of these deaths was due to cardiac complications (36, or 42.69 per cent). Pulmonary complications accounted for 25.82 per cent of the deaths.

J. P. GREENHILL

Borras, P. E.: Surgical Treatment of Uterovaginal Prolapse, *An. Catedra d clin. ginec.* 2: 97-103, 1943.

The author states that no fixed procedure can be followed in operative treatment of vaginal and uterovaginal prolapse, for various factors must be considered: The condition of the tissues, grade of lesion, patient's age, with all its subsidiary factors, constitutional type, economic status, etc. In his experience, there are four fundamental facts to be ascertained: whether or not a retroflexion has to be corrected; whether or not a cystocele requires dissection of the fascia and reefing of the pubovesico-uterine ligaments; whether there is elongation of the cervix; whether a posterior colpocoele requires repair, and if so, its extent.

These types of cases are discussed in connection with the Halban and Fothergill operations. The author believes that both are superior techniques, and that the results are practically identical, but for simplicity of technique and minimal risk, he prefers the Fothergill procedure. He comments that his own statistics would seem to contradict this, since he reports two deaths with the Fothergill, and none with the Halban operation. However, one of these patients was aged and died from syncope twelve days after operation, while the other got out of bed, against the surgeon's instructions, and suffered a severe hemorrhage, necessitating removal of the tampon by the attending physician, with separation of sutures and subsequent infection.

Two series of cases from the Hospital Español and the Catedra de Ginecologia are presented, a total of 632. Operation was carried out in 589; the Halban technique was used in 293, and the Fothergill in 145. Sixty-four hysterectomies for prolapse and 28 ward cystopexies were also done, and the remainder of the operations was performed by other techniques or was done before the Halban operation was used.

The surgical results are entirely satisfactory with either the Halban or Fothergill operation. There are practically no recurrences and the patients generally exhibit great improvement. There were only five cases of recurrence after the Halban, and two after the Fothergill. Postoperative complications were: Hematoma of the lateral vaginal wall, 1 case (Halban); hemorrhage, 2 cases (Halban); cystitis, 4

cases (2 Halban, 6 Fothergill); febrile course, 3 (2 Halban, 1 Fothergill); phlebitis, (Halban); cardiovascular failure, 1 (Fothergill).

All types of anesthesia were used, but spinal anesthesia with novocain and infiltration of the vaginal tissues with adrenalin solution was used in the majority.

J. P. GREENHILL

Labor, Complications

Ferrari, R. A.: Present Conception of Treatment of Obstetric Shock, *Obst. y ginec. Latino-Americanas* 1: 479-485, 1943.

Obstetric shock is a syndrome resulting from depression of many functions—neuromuscular, glandular and visceral, but reduction of effective circulating volume of blood and of arterial tension is of basic importance, and treatment must be directed toward combating this.

Transfusion of whole blood is the best treatment for patients whose shock results from quantitative loss of blood, and who need both plasma and blood cells. Transfusions of whole blood are contraindicated in patients whose shock is the result of loss of plasma (obstetric operations with prolonged visceral exposure), because of hemoconcentration, and administration of plasma alone is more beneficial.

Blood plasma is the substitute which is now accepted as most satisfactory and effective. It meets the prime necessity of restoring circulating volume promptly. It is physiologic and stable, easily transported and prepared easily and quickly.

As complementary medication are the administration of analeptics with peripheral and central action; warming of the patient; lowering of the head; oxygen and morphine in cases with excitement or pain, intravenous injection of warm saline solution. Heart stimulants are ineffective, as are also subcutaneous or intramuscular fluids, because the peripheral circulation is greatly retarded. Preseverance in treatment and supervigilance of the patient with shock are necessary to obtain satisfactory results in this condition.

J. P. GREENHILL

Macleod, A. J.: Manual Dilatation of Pelvis, *Brit. M.-J.* 2: 484, 1943.

The author refers to his previous report (1936), of a case in which the pelvic girdle was dilated to avoid the death of a patient in parturition. He now reports four cases. They were primiparas with minor degrees of pelvic contraction, complicated by early rupture of membranes and showed signs of fetal distress after protracted labor and at a time when "the size-relation of the head and passages was unfavorable." He writes with reference to technique: Leverage must be from bone to bone, and may be done with the fingertips on one and the knuckles, or the back of the hand against the other. The pressure should not be long continued—a few seconds, and should move from one pair of points to another. The fingertips may stretch the taut ligaments by stroking across their axis.

The author concludes that manual dilatation of the bony pelvis can be safely and successfully used to minimize birth trauma and that it is especially indicated in cases of slight disproportion which have to be delivered at an unfavorable stage.

FRED L. ADAIR

Item

The Practical Clinical Importance of the Rh Blood Type and a Project for the Collection and Preparation of Suitable Rh Typing Serum

In 1940, Landsteiner and Wiener discovered the new blood type—Rh, present in 87 per cent of the white population and absent in 13 per cent. At first, it was thought to have no practical or clinical importance. However, it was soon demonstrated by Levine and by Wiener that Rh-negative individuals (lacking this Rh agglutininogen) might, under certain circumstances, develop immune antibodies against the Rh factor and suffer serious consequences from the action of such anti-Rh agglutinins.

Abundant evidence has been collected by now to show that anti-Rh agglutinins may be developed in Rh-negative males and females as the result of one or more transfusions with Rh-positive blood, and in women, by repeated pregnancies involving an Rh-positive fetus (this blood type being inherited as a dominant characteristic from the father).

Recognized intragroup transfusion reactions due to Rh incompatibility have apparently been quite rare in civilian practice. This does not imply that Rh-negative individuals who receive Rh-positive blood fail to develop antibodies, in most instances. On the contrary, data from the Blood Grouping Laboratory of Boston suggest that many such recipients develop weak agglutinins. Subsequent transfusion reactions are fairly mild unless numerous transfusions are given and strong agglutinins develop. Probably the most important reason for failure to note a higher percentage of hemolytic transfusion reactions of this type is that multiple transfusions are the exception in civilian practice. More than 95 per cent of the transfusions are single infusions of blood. In contrast to this, in the treatment of members of the Armed Forces, multiple transfusions are exceedingly common, and therefore transfusion reactions in the 13 per cent of the population which are Rh negative are quite likely to become more frequent and severe, thus interfering with benefit from the procedure, with speed of convalescence, and even with eventual recovery. This has been borne out by statistics available from the British Armed Forces.

Because of the increasing availability of plasma and whole blood, and the attempt to diminish maternal mortality due to hemorrhage and puerperal sepsis, transfusions are now given to patients in obstetric services much more often than in days past. In contrast to the experience with medical or surgical cases, a first transfusion of Rh-positive blood to an Rh-negative mother, who has been sensitized by pregnancy with an Rh-positive fetus, may be followed by a fatal reaction. Also an Rh-negative woman of childbearing age, given Rh-positive blood, will be sensitized, develop anti-Rh agglutinins, and if she then has a pregnancy involving an Rh-positive fetus, the child will develop erythroblastosis, often of the most severe type.

To sum up the accumulated facts, it may be stated that Rh incompatibility is of practical importance under the following conditions:

1. Rh-negative recipients, men and nongravid women, who receive repeated transfusions of Rh-positive blood may have intragroup hemolytic transfusion reactions. Such reactions do not occur following the first transfusion, but after a suitable interval for the development of antibodies, further transfusions produce signs of increasing hemolytic reaction with jaundice, anemia, and finally anuria.

2. Rh-positive infants born to mothers who have anti-Rh agglutinins may show varying degrees of hemolytic anemia of the newborn, or erythroblastosis fetalis. The severer forms are characterized by late fetal death with congenital hydrops, and icterus gravis. In this situation, Rh typing of mother, father, and child are of diagnostic value, and demonstration of anti-Rh agglutinins in the mother may fix an otherwise questionable diagnosis.

3. Serious and even fatal hemolytic transfusion reactions may result from the *very first transfusion* in Rh-negative women who have been sensitized and have developed anti-Rh agglutinins through pregnancies.

4. The use of Rh-positive blood for transfusion of Rh-negative women even for the first time may initiate the formation of anti-Rh agglutinins and produce erythroblastosis of a severe or fatal form in their Rh-positive offspring.

For the above reasons, it has become apparent that Rh typing should be carried out for:

1. Recipients of whole blood or of resuspended red cells, especially if multiple transfusions are contemplated, in order to avoid giving an Rh-negative individual blood that is not compatible according to this factor, i.e., Rh-positive blood.

a. It is most important to type recipients of multiple transfusions or persons having a history of previous transfusions.

b. Donors and stored blood should also be typed for Rh, so that suitable blood is available for the Rh-negative individuals.

2. Any woman whose history suggests the possibility of erythroblastosis in the fetus—either by one or more stillbirths, or infants born with hydrops, jaundice, or anemia, before even a first transfusion is given, since a fatal reaction may occur.

3. Women of childbearing age before transfusion, since Rh-negative women given Rh-positive blood may be so sensitized that future pregnancies will result in dead or damaged infants.

4. Babies born with jaundice and anemia, in order that their recovery may be facilitated by transfusion with Rh-negative blood.

The Military Services require Rh-typing serum even more urgently than do the civilian hospitals, since multiple transfusions are so much more common in military institutions, and also because obstetric services are expanding in military establishments. Not only is it necessary to have such serum for the typing of recipients, but also for the typing of prospective donors, either for the Rh-negative patients or for a donors list or for banked blood for emergency use. The most serious difficulty in this connection has been the relative paucity of available serum. The reasons for this are threefold:

1. Experimental or animal serum is difficult to produce and gives agglutinations that are unreliable or difficult to read by the average technician.

2. High-titered serum of human origin occurs chiefly in women recently delivered of erythroblastotic infants, and even here it is found in only one of 20 such women, or one in 4,000 deliveries.

3. Such high-titered serum may be highly specific (70 per cent instead of 87 per cent positive reactions), and therefore may not be useful for general Rh testing. This makes the occurrence of high-titered useful serum about one in 6,000 deliveries.

For these reasons other means of increasing the supply of Rh-typing material seemed required. It had been noted that low-titered anti-Rh serums were much more commonly found (ten times as often) than the high-titered agglutinins. However, this material was not safe for general laboratory use because the tests obtained were not clear-cut and many negative results occurred with known Rh-positive cells. Through the cooperation of the Department of Physical Chemistry of the Harvard Medical School such low-titered serum was concentrated into a globulin fraction yielding good typing results. This opened the possibility of utilizing the more abundant supply of serum containing low-titered Rh agglutinins and thereby possibly meeting the need for Rh-typing material.

Accordingly, a project was started under contract from the Office of Scientific Research and Development of the Committee on Medical Research for the collection and preparation of Rh-typing serum. During the past six months, meetings have been arranged with obstetricians, pediatricians, and clinical pathologists in all the large medical centers, and the facts regarding the need for Rh-typing serum have been presented. It has been suggested that they send a few c.c. of blood on any patient known to them to have had a baby with erythroblastosis or possible erythroblastosis (including late fetal death of undiagnosed cause) delivered within the last two years. If the serum, by *in vitro* tests, shows a useful amount of anti-Rh agglutinin, the physician is notified and requested to obtain from the patient 100 to 500 c.c. of blood to be shipped promptly. Such material is pooled for concentration of the anti-Rh agglutinin, thereby producing a useful typing globulin. Seventy per cent of the resulting serum is set aside for use by the Military Services, and thirty per cent is credited to the hospitals or physicians contributing in this enterprise. Such a credit can be drawn on immediately in the form of standard Rh typing serum, so that any hospital or laboratory may have its own material without delay. Special preaddressed containers and test tubes are being sent to all physicians and hospitals cooperating in this project so that shipment of specimens may be expedited. Also collecting bottles and preaddressed containers for sending blood serum via air express, collect, are obtainable on request.

Only through such a cooperative enterprise for obtaining large amounts of Rh-typing serum does it seem possible to meet the urgent and increasing needs of the Military Forces, as more whole blood is being used; also by this means it is hoped to supply the immediate and future demands of obstetric and general hospitals.

All requests for information and for material should be addressed to Dr. Louis K. Diamond, Blood Grouping Laboratory, 300 Longwood Avenue, Boston 15, Massachusetts.

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Original Communications

A CONSIDERATION OF THERAPEUTIC ABORTION*

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(From the Margaret Hague Maternity Hospital)

THE seriousness of abortion as an ever present problem, and factor in unnecessary puerperal mortality and morbidity, need hardly be reiterated. Thus Taussig says, "abortion is probably the most wasteful of known ills in its expenditure of human life and human health."

Certain very special difficulties are involved in undertaking an attack upon this problem. And I shall not attempt a full consideration of it, with all its economic, sociologic, legislature and medical considerations. But it seems to me that most of us shy away from some of the obvious implications of the situation.

Our whole profession enjoys regarding itself as a highly moral and ethical group. We complacently assume that any individual who is admitted by scholastic attainment and satisfaction of legal requirement, into that group, is per se endowed with the honor and the high moral and ethical principles, which we like to think characterizes each one of us in our several attitudes toward our work.

We therefore, rather shamefacedly deplore the tremendous incidence of what we offhandedly characterize as "illegal" abortion with a more or less definitive implication that by far the larger number of such abortions are performed by nonmedical individuals, or by a small number of unworthy persons, who by some misadventence, have been admitted into the sacrosanct ranks of those to whom proper moral and ethical standards in the practice of their profession has been providentially inborn in our own persons!

*Read at a meeting of the New York Obstetrical Society, March 14, 1944.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

My sole thesis is that we, as individuals and as a united profession, must maintain in our approach to this problem, a basic moral and ethical attitude. Whatever are our several divergencies of thought concerning it, all agree that only adherence to individual integrity of purpose will prevent the absolute degeneration of any system of remedial action advocated. Thus Rongy, one of the most radical American commentators says, "I have made certain of holding inviolate the dictates of conscience, both as a practitioner of medicine . . . and as a true believer in the ideals of liberalism," and says that he is deeply grateful that this combination has been possible for *him*. Thus he clearly implies the difficulty of most men in so holding conscience inviolate.

But an alarm clock cannot strike without being set to a definite time. The warning bell of conscience cannot ring without a definitive ethical standard to which it is geared. The importance of such a standard just at this time is emphasized by the statement that in connection with the accelerated war program of medical education, many individuals of less desirable moral calibre are likely to be admitted to our medical schools.

But were I today the graduate of any nonsectarian medical school in the country, what positive instruction would I have had at any point in my career as an undergraduate student which would tell me just whether and why I had any right to do abortions, and what constituted the right and wrong of such situations? In other words, what positive guidance would I have had as to the moral and ethical values involved in abortion?

I am afraid I would be very much at a loss. My several instructors would not have spent a great deal of time impressing these matters upon my embryonic medical mind. I would not, as such a new graduate in medicine, possess any strong bulwark against the temptation to indulge in the practice of abortion in a manner and to an extent which would make me a stench and a pariah in the opinion and estimation of the members of my chosen profession.

If one desired to inculcate any system of ethics, it would seem necessary to start with some very fundamental definitions and then to characterize acts done in violation of these definitions as unethical, and unlawful. Therefore, let us attempt a statement of clear, workable concepts. Abortion itself is sometimes defined as any termination of pregnancy prior to the natural termination of complete, or full-term, gestation. Such an all-inclusive definition, however, brings into indiscriminate consideration situations having no identity of moral significance. I shall accept a definition of abortion as "the termination of a previable uterine pregnancy; i.e., the expulsion or extraction of a live or a stillborn fetus before the seventh month (twenty-eighth week) of gestation," (*Childrens' Bureau, U. S. Department of Labor*), or the essentially identical phrasing proposed by Taussig as the legal definition,

"the destruction of the life of the child or its expulsion from the mother's womb, before it has become viable; that is, able to sustain life after its birth." It will be observed that these definitions express nothing as to the ethical propriety of abortion. And yet, unless there be some definition along moral lines, there can be no distinction whatever as between abortion which is legitimate and that which is not legitimate, or "criminal."

The common use of the phrase "criminal abortion" in literature and texts would imply that there was such a distinction between legitimate and illegitimate abortion in the law, and that we had only to turn to the law to receive the guidance which I am implying is desirable and salutary. Strangely enough, this is not so. The law in most of the jurisdictions of this country is based upon the old English common law. Under this law the unborn child, prior to quickening, has no entity, no legal existence, therefore no rights, therefore no possible violation of its rights, therefore no possibility of a crime against it whatsoever. From the standpoint of the fetus, there can be no crime involved in the destruction of its existence. In general this concept holds, and is embodied, in existing law in the several state jurisdictions in this country.

The laws of the several states do indeed contain restrictions as to the performing or procuring of abortions. Most of them contain exceptions designed evidently to permit its employment as a therapeutic procedure. The terms of such exceptions, however, are so astonishingly loose in the vast majority of cases as to actually constitute little deterrence. For instance, New Jersey law says, "any person who maliciously, or *without lawful justification*, with intent to cause or procure the miscarriage of a woman then pregnant with child, shall administer to her, prescribe for her, or advise or direct her to take or swallow any poison, drug or medicine or noxious thing; or who maliciously or without lawful justification, shall use any instrument or means whatever, with the like intent, shall be guilty of a high misdemeanor. . . ." It will be noted that there is no definition of "lawful justification," nor any specification of the function of the physician in relation thereto. New York law forbids prescription, supplying, administering, advising, or causing a woman to take any medicine, drug, or substance, or using or causing to be used, any instrument or other means, with intent thereby to procure the miscarriage of a woman, *unless the same is necessary to preserve the life of the woman, or of the child with which she is pregnant*, and sharply increases the seriousness of the crime if the woman or her "quick child" dies. Here again, there is no specification of the basis of determination of the necessity for life salvage, nor restriction of the actual act to physicians.

Very few jurisdictions require that the determination of the necessity of abortion to save the mother's life must depend on medical men, or that the procedure when so determined, be carried out by medical

men. Only four jurisdictions recognize preservation of the mother's health as justifying abortion.

Mississippi exempts cases "advised by a physician to be necessary," without specifying the ground for such necessity, and with no restriction as to who may do the procedure.

The most specific laws are that of New Mexico, which makes attempted or actual abortion a felony "provided, however, an abortion may be produced when two physicians licensed to practice in the State of New Mexico, in consultation, deem it necessary to preserve the life of the woman, or to prevent serious and permanent bodily injury."

The District of Columbia makes the procurement of miscarriage of any woman unlawful, "unless when necessary to preserve her life or health, and under the direction of a licensed practitioner of medicine." This phraseology would apparently make it somewhat ambiguous as to whether the procedure actually has to be carried out by a licensed practitioner.

In Maryland the law provides "that nothing contained therein shall be construed so as to prohibit the production of abortion by a regular practitioner of medicine when, after consultation with one or more respectable physicians, he shall be satisfied that the fetus is dead, or that no other method will secure the safety of the mother."

If we cannot depend on the civil law for guidance as to ethical and moral principles involved, there must be that in the several codes of organizations like the American Medical Association and the American College of Surgeons to constitute a sufficiently definite and specific guide. If there are such, I have been unable to find them.

Yet certainly if in general the indiscriminate incidence of abortion of all types is a serious sociomedical problem, it becomes essential to adopt certain definitions based on secular ethical standards determined by the preponderance of opinion of the high-thinking members of our profession.

Of course it would be possible to find such ethical standards existent in the teachings of several religious bodies. It is not felt desirable however to resort to the direct teachings of any particular, or any several, such organizations. It is presumed that any ethical standards adopted by present-day medical or legalistic bodies would not lack the influence of organized religion on the background out of which such items of a moral code might arise. But it is unfortunate that there is enough difference in attitude between the several currently extant religious congregations, as to make specific religious teachings in respect to minutiae of doctrine, a difficult and insecure basis for approach to certain problems. In the present thought it is believed that the religious approach should be sedulously avoided.

What are the bases upon which one may erect an ethical standard to apply to this problem? It seems to me that they are very simple:

1. Physiologically, the unborn human being at any time after conception is an entity with all the potential life possibilities of any other creature.

2. It is entitled to the protection of those life potentialities as surely as is any other human being.

3. It is the duty of the profession to save and conserve human life. Effort to save human life however, must not deliberately and of itself jeopardize the life of another individual, nor even the same individual. One will recall numerous instances of the discussion of the propriety of particular operative procedures designed to directly save human life, the discussion revolving around the question as to whether an especially high immediate operative mortality-risk justifies the use of such procedure or not. In other words, it is recognized that it is not legitimate, even with the object of direct salvage of human life, to employ a means of therapy so formidable that its inherent risk is significantly large in relation to its potential salvage possibilities.

With these very simple basic considerations as the foundation for our ethical structure, the deliberate and intentional interruption of fetal life and growth is actually murder. If this is so, then abortion is never justified any more than any other murder is.

Child sums this up as follows: By *common law* the fetus in utero is not protected before quickening. But "Life is present from the time conception first occurs . . . the fetus is a living, independent being, has the right to exist which is common to all human beings, and is entitled to the protection of the State. . . . The direct taking of an innocent life is always murder . . . at whatever stage of existence it is committed."

But all religious and legalistic codes do admit that murder is sometimes justified. For instance, while the church of Jesus Christ cannot condone the mass murder which is war, it cannot be so unrealistic as to regard as a murderer every soldier who kills in war. Any individual, even under our modern laws, may kill an aggressor on his life, on that of one near and dear to him or, under some circumstances, a violator of his property rights, or an intruder on his domicile. Organized society in many jurisdictions reserves the right to murder convicted individuals as a preventive and punitive measure against certain crimes, especially murder itself.

But now note that all such so-called "justifiable" murder is surrounded by special safeguards as to the authenticity and factual reality of the circumstances attending it. History does not condone an act of war unless it be justified by actual hostile aggression.

Every circumstance relative to the basis of legal murder by execution is carefully scrutinized on the basis of a consensus of evidence and opinion *before* that murder is committed.

Where justifiable murder cannot be carefully considered beforehand, as when a policeman kills an assailant in alleged self-defense, the law insists on reviewing the circumstances *afterward*. If such review showed

that the *imminence of risk to his own life* did not justify the murder of his assailant, the killer himself may stand in jeopardy of punishment for destroying life without justification.

Is the murder which is abortion ever justifiable? The considered, honest opinion of many, probably a majority, of medical practitioners of high scientific attainment and unimpeachable moral character, is yes!

This opinion is based on the fundamental idea that under some circumstances the existence of pregnancy is a definite, direct and imminent jeopardy to the mother's life; that termination of the pregnancy is the only direct therapeutic resource to avert that jeopardy; and that therefore the murder of the fetus which such termination constitutes, is justified.

If this idea be valid, and such murder therefore sometimes justifiable, certainly it should be restricted in the same manner as is other "justifiable" murder.

First, like legal execution-murder, its justification must be determined, by careful weighing of the evidence, by more than one competent and competently authorized person. It is obvious, that for purposes of the highest justice, a maximum rather than a minimum number of such persons should participate in the decision.

Second, the evidence must show that the pregnancy threatens the life of the mother *imminently*. This question of imminence of lethal risk to the mother seems to me the *crux* of the consideration of the evidence. There is wide and increasing tendency to include in the evidence justifying abortion:

a. Remote threat to the mother's life, and hence;

b. Threat to the *health* of the mother. Thus Taussig repeatedly makes the plea for "broader indications for therapeutic abortion."

Such broadening of indication for justifiable or "therapeutic" feticide tends to practical removal of all deterrent to this practice. It is obvious that individual opinion as to "threat" to the mother's health may vary within the widest limits. In fact, it has been conceived that *any* pregnancy is a threat to the health of *any* woman. In other words, every pregnancy necessarily entails some inherent risks. If these risks be considered as "threats to the mother's health," there would be no bar to the induction of abortion in any pregnancy. But Lord Riddell, eminent British jurist quoted by Taussig, says, "a woman who becomes pregnant must be prepared to undergo the ordinary discomfort of pregnancy and to take the ordinary risks. Therefore, the practitioner must not be influenced by the abjurations of the patient to relieve her of these."

So much have these secondary considerations become acceptable as justifying "therapeutic" abortion, that we find in some of the outstanding obstetrical clinics in this country, they are actually being done in a proportion as high as almost 3 per cent of deliveries.

TABLE I. INCIDENCE OF THERAPEUTIC ABORTION IN A FEW REPRESENTATIVE CLINICS (EXCEPT WHERE NOTED, FROM OFFICIAL REPORTS OF THE RESPECTIVE INSTITUTIONS)

| NAME | PERIOD | NO. ABORTIONS | NO. DELIVERIES | PER CENT | RATIO |
|--|--------------|---------------|----------------|----------|----------|
| Johns Hopkins | 1941 to 1942 | 55 | 1903 | 2.88 | 1:35 |
| Woman's Hospital, New York | 1941 | 21 | 1798 | 1.20 | 1:85 |
| Bellevue | 1942 to 1943 | 20 | 1712 | 1.16 | 1:86 |
| Sloane | 1942 | 12 | 1744 | 0.69 | 1:145 |
| New York Lying-In* | 1942 to 1943 | 43 | 6561 | 0.66 | 1:153 |
| Chicago Lying-In† | 1931 to 1939 | 134 | ---- | 0.51 | 1:195 |
| Margaret Hague Mater- nity Hospital | 1931 to 1943 | 4 | 67000 | 0.006 | 1:16,750 |

*Personal communication, Dr. Gordon Douglas.

†Hesseltine, H. C., Adair, F. L., and Boynton, M. W.: AM. J. OBST. & GYNEC. 39: 549, 1940.

I very sincerely do not desire to impose on others the dictates which might appeal to my own conscience; nor to assert that abortion-murder is never justified. But I submit that in clinics charged with the primary duty of training undergraduate students of medicine there should be recognition of responsibility for inculcating the moral and ethical phases of that training. Where "therapeutic" abortion is so freely and frequently resorted to, there can hardly be any emphasis laid on the abhorrence of abortion in general. If it be part of the responsibility of such teaching clinics to establish in their students proper respect for the age-old ethics of medicine, they can hardly acquit themselves of this duty by slackening the standards by which they resort to abortion.

From our own experience I believe that by stricter adherence to the ethical basis I have tried to outline, and with a closer scrutiny of the so-called medical indications for abortion, the actual necessity therefor would be very much reduced.

Among the more common "indications" for "therapeutic" abortion are:

1. *Hyperemesis Gravidarum*.—This condition, where modern hospitalization and therapeutic resources are available, is almost always curable without abortion. In the last ten years we have treated 290 cases of this condition, of whom none has died, and one only has been aborted. This woman had had one previous pregnancy, 1936, during which there were two hospital admissions for hyperemesis, but she went to term and delivered a healthy 3,340 Gm. infant.

In her second pregnancy, 1939, she was again admitted at the fourth week with hyperemesis characterized by continuous vomiting, marked weight loss, persistent acetoneuria, blood uric acid increased to 4.6, icteric index 46.5, icterus of sclera and skin, failure of improvement after two weeks' intensive treatment.

Therapeutic abortion by curettage at 6 weeks' gestation. Good recovery.

In her third pregnancy, 1940, she presented an almost precisely similar syndrome, complicated by severe gingivitis and parotiditis. She was discharged on her thirty-third hospital day, and at term delivered spontaneously a healthy 3,790 Gm. girl.

In the light of her last experience, it may legitimately be questioned whether the abortion of her second pregnancy had been necessary.

2. *Toxemia of Pregnancy.*—While premature induction of labor is not infrequently necessary, this condition seldom occurs early enough in the course of pregnancy to necessitate consideration of therapeutic abortion as we have defined it. Our own experience would not lead us to believe that a mere history of prior acute pregnancy toxemia even in its gravest forms, justifies abortion of a succeeding pregnancy. Thus, of 153 women followed for varying periods up to 8 years who had suffered an original eclampsia, 90 had 143 subsequent pregnancies in the observation periods; the stillbirth rate was higher than the average, but in more than half the pregnancies, the women entirely escaped any degree of toxemia and only two had a repetition of eclampsia.

3. *Fixed Hypertension.*—Pregnancy in such cases presents the necessity for urgent consideration of abortion, for this condition not only spells certain imminent dangers in the course of pregnancy, but the pregnancy sometimes accelerates the malign course of the disease, and may thereby definitely shorten the mother's ultimate life expectancy.

But there must at least be careful individualization of each case. No ukase against the children of all hypertensive mothers may be indiscriminately applied. The most severe cases of this group generally abort spontaneously. Their life expectancy is so insecure that any general percentage probabilities applied to them would result in only inconsiderable differences in duration thereof.

On the other hand, Chesley's review of very carefully collected data in a large group over a considerable period of time indicates that approximately one-third of even these severe cases are not prejudiced by pregnancy in their subsequent condition and course. There are no criteria available for predetermining which individual will be so exempt from aggravation of her condition by pregnancy. We have observed numerous cases in which careful and prolonged hospital management has resulted in successful outcome of the pregnancy without apparent aggravation of the patient's condition. It is almost a certainty that more general application of properly prolonged medical treatment would greatly increase the proportion of these cases which could experience pregnancy with relative impunity. Much the same considerations apply to nephritis.

One of our four abortions was done in a patient who showed definite renal disease in one pregnancy, which she successfully completed. She almost immediately again became pregnant, showed even more severe and progressive renal involvement very early in the pregnancy, and was submitted to abdominal hysterotomy and bilateral salpingotomy at four months, with good immediate recovery.

Another of the cases in which we did resort to abortion and sterilization was a 37-year-old multigravida three months pregnant with a marked hypertension, heavy proteinuria and severe edema. She recovered, but remained permanently hypertensive as long as she could be followed.

The fourth case in our abortion series was a woman who had four pregnancies in 7 years, the first uncomplicated, the second characterized by severe pre-eclampsia, the third by severe pre-eclampsia with nephritis, the fourth by extreme hypertension and nephrosclerosis. In each of the last three pregnancies in which we handled her, she reported

too late for us to prevent or control the toxemia. In each case pregnancy was terminated almost as soon as she came under observation. The last time, it was terminated at 14 weeks, thus coming under our definition of abortion, but she died shortly afterward of uremia.

It is thus seen that three of our four abortions were done for hypertension and/or nephritis. In one instance, it failed to avert death in a woman in whom repeated pregnancy manifestations of a probably consistently and rapidly progressive process had reached terminal seriousness. It is probable that prevention of her last two pregnancies might have prolonged her life. But it is certain that in her last experience, although her life was imminently threatened by disease, the abortion did not save her, nor could it probably have done so if employed earlier in that pregnancy.

4. *Heart Disease*.—In this disease our experience leads us to believe that in only the gravest cases; i.e., those of Type IV, in actual failure, is there justification for abortion. Such cases form only about 1.5 per cent of our cases. Any cases *not* in acute failure may be prevented, in almost 98 per cent of cases, by good management, from going into failure. The case in failure is of course, eminently *not* a fit subject for any surgical procedure. It may be conceived that very rarely a case seen in decompensation, early in pregnancy might justifiably be aborted after recovery of compensation, but here again, the risk of abortion must be weighed against that of recurrence of decompensation under good management. While our deaths from heart disease, like that of The New York Lying-in Hospital, are about 10 per cent of all our deaths, it is principally made up of cases admitted in decompensation following inadequate management either in our own or other hands. We have not found it necessary to do any abortion for heart disease.

5. *Pulmonary Tuberculosis*.—No more bitter nor extensive controversy perhaps has ever raged than that over the question of the influence of pregnancy on pulmonary tuberculosis. Voluminous references may be adduced on either the radical or conservative side of the application of abortion in the tuberculous pregnant woman. But it may justly be said that the last decade has witnessed a very decided swing to conservatism. Two of the most recent reviews, one British, and one American, fall into this group. I am not prepared to offer any definitive conclusion from our own experience, because a study by Robert A. Cosgrove, of our own staff, and Alfred Kruger, of the staff of the Hudson County Tuberculosis Hospital, was interrupted by war exigencies. But it has been my conviction for many years that, crudely put, the tuberculous patient susceptible of arrest can stand pregnancy, she who will not arrest will not be seriously accelerated in her course by pregnancy. This is especially true since the more perfect evolution of the surgical means of controlling tuberculosis. These resources may all be applied as indicated, during pregnancy.

In all of these conditions adequately intensive and prolonged medical treatment of the medical cases which happen also to be pregnant, would result in little change caused by the pregnancy in the natural history of the medical conditions.

Many other diseases complicated by intercurrent pregnancy will pose problems. In some, the urgency of surgical indication in the treatment of the disease per se, will necessarily and properly entail inevitable secondary sacrifice of a pregnancy.

In others, the dire and imminent threat to life incident in the disease itself gives primary impulse to rid the battling maternal organism of the

presumed embarrassment of pregnancy. Unfortunately, in such a circumstance, the performance of abortion all too frequently avails not at all in improving the prognosis. It may sometimes add a very direct danger of its own. For in spite of the unbelievably favorable statistics published from Russia, and the assertion of some authorities that abortion when properly done, is at least immediately innocuous, general experience indicates that such operations are not without considerable and direct risk in themselves. Thus, in one first-class American clinic 5.5 per cent of the therapeutic abortions died as a direct result of that procedure. Greenhill says, "We consider the operation of induced abortion one of the most dangerous in obstetrics."

The indirect risk of abortion in respect to numerous sequelae is part of all experience, and is significantly reflected in the vast experience of the Russians.

The confines of this paper do not permit discussion of the sociologic and economic phases of abortion. In what has been said above in relation to proper hospitalization and management of handicapped pregnant women there is, however, necessarily, implication of the necessity of increased socio-economic assistance to these folk. Such assistance therefore, becomes a primary necessity of any program for the control of the abortion evil.

Summary

1. The medical profession, from the nature of its work and obligations, is, and must continue to be, a highly ethical group.

2. A high sense of this ethical obligation must be thoroughly instilled in medical men during their undergraduate experience.

3. The responsibility for this ethical training resides in medical teaching facilities. This responsibility entails organized positive efforts toward its fulfillment.

4. Nowhere does this ethical sense have a more direct bearing than in relation to abortion.

5. Widespread and indiscriminate abortion is a major factor in puerperal mortality and morbidity, recognized by all medical and social students.

6. It is believed to be best controlled by retention of the ethical recognition that the fetus is a human individual with all the potentialities of every human being, and that its destruction is murder, only justifiable in the most extreme circumstances involving direct and imminent threat to the mother's life.

7. And that as a corollary, improvement in the whole situation must depend most importantly on the wide development of one of the Four Freedoms which is the goal of our national development, that of Freedom from want.

8. And, that in the preservation of the ethical sanctity of fetal life, and the development of this Freedom in all its phases, lies more hope of eventual betterment than a reversion to the amoral and unethical

plane of the most primitive and debased societies which has been exemplified with highly questionable success in Russian experience of the last two decades, and which has been essentially proposed by some thoughtful and sincere commentators amongst us.

9. And finally, that it is the duty of representative special medical bodies to formulate and supply a specific code for the ethical guidance of the members of our profession in relation to this problem.

NOTE: Appreciation is expressed for interest and help in the preparation of this essay to Leon C. Chesley, Ph.D., to Henry P. Wager, M.D., and to Dr. Benjamin J. Elwood, of the Hudson County Tuberculosis Hospital.

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Discussion

DR. MEYER ROSENTHAL.—Dr. Dickinson has made a very excellent plea: Shall we have the courage of our convictions in this matter of abortion? At the present moment, we are governed by the law and it is with this in mind that I would like to acquaint you with the law at this time and with the contemplated new law in New York State. There are two procedures to which the doctor doing an abortion is subject: One is the code of civil procedure which requires two consultants; and the penal code which lays down certain definite limits as to when an abortion can be done; this section of the penal code is now to be repealed. The new law, however, has not been passed as yet.

The contemplated law defines abortion and therapeutic abortion, and punishment of one who performs a nontherapeutic abortion. An abortion is the interruption of intrauterine pregnancy before the period of viability (up to 28 weeks of gestation) is reached.

A therapeutic abortion is the artificial interruption of an intrauterine pregnancy before the period of viability (up to 28 weeks of gestation) is reached where the continuance of such pregnancy would jeopardize the life of the woman or so aggravate the physical or mental disease from which she suffers as seriously to impair her health or threaten her life. It may be performed only by a physician duly licensed in the state of New York and only in a hospital recognized by the Department of Social Welfare of New York State, or the Department of Health of New York State, or approved by the American College of Surgeons and/or the American Medical Association, after written opinions as to its necessity have been obtained from two competent, qualified, and recognized consultants in the respective specialties involved, which said written opinions shall be incorporated in the records of the hospital.

A person who prescribes, supplies, or administers to a woman or advises or causes a woman to take any medicine, drug, or substance, or uses or causes to be used any instrument or other means with the intent of producing an abortion other than a therapeutic abortion as above defined, is guilty of a felony punishable by imprisonment in a state prison for not more than four years.

A person who as a consultant willfully makes a false or misleading certificate is guilty of a misdemeanor punishable by imprisonment for a term not to exceed one year and a fine not to exceed five hundred dollars or both for the first offense, and for a second and subsequent offense, such person shall be guilty of a felony punishable by imprisonment in a state prison for a term of not more than three years, or a fine not to exceed one thousand dollars or both.

As far as another objection which Dr. Cosgrove brought out about the entity of the offspring from the moment of conception is concerned, I believe that in California there is a decision that the child immediately after the moment of conception may inherit; in other words, the child is an entity. The case in point was where an inheritance was left to be divided among children and grandchildren and it was a question whether a share of this was to go to this offspring conceived a week or month before the death of the maker of the will. The court ruled the child was an entity and as such entitled to inherit.

DR. WILLIAM E. STUDDIFORD.—I have been somewhat responsible for the therapeutic abortions performed at Bellevue Hospital in the last ten years. Since I note that the incidence as given by Dr. Cosgrove is moderately high, I would like to say a few words in regard to these cases. I believe that, on the whole, we feel very much as Dr. Cosgrove does. On the other hand, we are a little more inclined to widen our indications. In regard to the specific indications that Dr. Cosgrove mentioned, I do not recollect any case being terminated at Bellevue Hospital in the last ten years with a diagnosis of hyperemesis. We have seen very few of such cases and those that we have seen have responded very readily to treatment.

In regard to the terminating of pregnancy in patients with a history of toxemia of pregnancy, we have to specify the variety of case we are talking about. It depends a great deal on whether it is a fulminating variety coming on with great rapidity toward the end of pregnancy and disappearing completely following the termination of pregnancy. Many of these cases do not do that. They come on earlier and the condition is present for several weeks before the pregnancy reaches term. We all know that these cases are very apt to be followed by hypertension, albuminuria and that they may recur and become worse in subsequent pregnancies and eventually impair the health of the mother. When such a background is present, further pregnancies are contraindicated.

The question of heart disease is a difficult one to settle. I think that every one of us feels that the cardiac patient who has had two or three children is better off if she does not have more children. Nevertheless, the Heart Association of New York City, has studied this very point; they have gathered together a large group of rheumatic cardiac patients who have gone through pregnancy and a similar group who have not, and they found that the average expectation of life in these patients is the same whether they have been pregnant or not.

In regard to pulmonary tuberculosis: in the last ten years we have been extremely conservative, especially in patients who have been brought to our attention after the third month of pregnancy. Most of these patients have been allowed to proceed with pregnancy and we have seen very few serious exacerbations of the disease as a result of allowing them to proceed.

We have been apt to include in the consideration of our indications for therapeutic abortion not only the patient's medical condition, but her surroundings and her social and economic status. If the conditions are favorable, we are inclined to allow her to continue, if not, we are more inclined to recommend termination of the pregnancy.

DR. GEORGE W. KOSMAK.—I feel like resenting somewhat the course which this discussion has taken.

In the minds of most of us I believe there is no doubt at all about the indications for therapeutic abortion which Dr. Cosgrove has outlined. These therapeutic abortions were done under the best possible conditions and with definite indications.

The abortion evil which has stimulated the passage of the bill referred to, does not constitute the crux of this situation at the present time. It is not the therapeutic abortion which bothers us so much as it is the criminal abortion. All the indications that Dr. Cosgrove outlined and which have been referred to by the other speakers are, I believe, generally accepted by the profession and in doing abortions for these conditions and on ethical grounds the legal requirements are probably pretty closely followed. But all these therapeutic abortions are not a "drop in the bucket" as has been indicated compared to the large number of other abortions which are done. I therefore resent Dr. Cosgrove's implication that therapeutic abortions, in a sense are "murders"; I think that is stretching the point a bit. However, I believe that most of the abortions that are done by the so-called professional abortionists are "murders." These professional abortionists have no altruistic

view as regards their work; they are doing it purely for the financial gain which comes to them and, therefore, we should be very careful in our discussion to bear this in mind. I think doctors as a class are thoroughly aware of the underlying factors which Dr. Cosgrove has so well outlined before they undertake abortions, but none of these factors is taken into consideration by the men who do these procedures merely for financial gain; therefore, I cannot quite agree with Dr. Dickinson that that type of abortion should be made a reason, if you might call it so, for any study of their methods because I do not believe that the profession as a whole would agree to be governed in its own procedures by the different tricks that these professional abortionists may have been able to put over.

DR. HOWARD C. TAYLOR, JR.—I think we are overlooking the extraordinary scientific experiment which Dr. Cosgrove has carried out in conducting a service with as low an incidence of therapeutic abortion as he apparently has succeeded in doing. It is not a case of having fewer therapeutic abortions than any of these other services to which he has referred, but being in an entirely different class from any other, as judged by his statistics.

I would like to ask whether in his opinion after this experience there were indications that should have been considered in addition to the four which he mentioned. I should like to be reassured that he believes there have been bad results in none of his mothers from reducing the incidence of therapeutic abortion to as low a point as he has been able to do.

DR. CLAUDE E. HEATON.—Dr. Cosgrove has presented us with a problem which as he points out is not only medical, but raises the question of ethics, morals and law.

So far as legality is concerned, people of integrity sometimes oppose a law impelled by motives which are entirely honest. Laws will not solve the problem of abortion.

What power is going to decide our morals, our ethics? The state? The church? If the latter, what church? A careful survey was made in an eastern industrial city: forty-one per cent of the group studied had no church affiliation at all. The faith of our fathers emphasized the individual's conscience. As reputable doctors we may safely follow the dictates of our own conscience when faced with the problem of abortion.

We, in this country believe the state derives its authority from the consent of the governed; we do not believe in a totalitarian state. Dr. Cosgrove rightly pleads for a change in society which will place the family on a firmer economic footing. Finally, in our attitudes toward the matter of abortions, there is all too often considerable downright hypocrisy.

DR. SAMUEL A. COSGROVE.—I would reciprocate Dr. Dickinson's kind personal expressions; I would express myself as most appreciative of the tremendous amount of work which he has done on abortion and many related subjects and testify to the utter honesty of his approach, the utter altruism of the self-sacrificing work that he has offered to the profession. I would also say that I willingly concede that he probably knows a good deal more about abortion than I do. I think, however, that most of his discussion was hardly pertinent to the paper because I was not discussing particularly the abortion evil. My only approach to the abortion evil was that unless we, in our application of definitive principles in our use of abortions which we consider legitimate, are absolutely careful and conscientious, we have no fountain head from which to approach any system of control of the whole abortion evil. I hope I have made that viewpoint clear. Inasmuch as I have tried to indicate the desirability and propriety of our application of an ethical standard for our work, I do not think that the testimony of profes-

sional abortionists is particularly applicable. I might take issue with some of his remarks. I do not think that illegitimate pregnancy necessarily always implies complete physical and psychical harm to the mother. He says that the law forbids us to see the experts work; maybe that is a good thing. He speaks of the refusal of organized medical bodies to investigate the work of professional abortionists. Well, we have twenty years of Russian experience. I won't take the time to read what appears to be the latest summary of the American viewpoint of the results of that vast Soviet experience, but it is available to you in the bibliography which will be published with the paper and was well exemplified in an editorial in the J. A. M. A. as long ago as eight years. It throws enough light on the broad results of indiscriminately applied abortion without the necessity of investigating the work of professional abortionists here. I sympathize with him in his attitude on the removal of the stigma of illegitimacy. Certainly we have no right, society has no right, to stigmatize the illegitimate child. It is an encouraging social indication that several states, including my own and I think New York and Pennsylvania, have removed the recorded stigma of illegitimacy from the transcripts of their birth certificates.

Dr. Rosensohn spoke of the proposed new law in New York. Clarification, as indicated by him in the new law, is badly needed because the present law is entirely indeterminate in the specification of the manner of determining the legitimacy of abortion. Of course, in regard to the California decision which he quoted and which recognized the entity of the earliest conceptions, that merely means that is one of the jurisdictions which has not in the past followed the old English common law workings; it is an instance of modern physiology rather than ancient legal concepts.

I was astonished to hear Dr. Aranow say that the medical profession was not concerned with determining ethical standards. Who is going to determine standards for us if it isn't ourselves? And since when does the medical profession not need to recognize ethical standards?

DR. HARRY ARANOW.—I meant ethical standards of taking human life—abortion. I was talking about whether or not it is legitimate for us to take human life.

DR. COSGROVE.—That is an important item in the ethics of medicine, and my plea tonight is for the profession to be specific in its own definition of its ethics and let the law follow it; let us guide the law and not be hidebound by the law.

The moment, however, that you permit social and economic considerations to enter the question of abortion, that is, legitimate medical abortions, you open the doors almost without any restraint at all. Because while you and I might estimate in any particular case that such and such a social and economic status justified abortion, the next person might admit just a little broader indication and the next fellow a still broader indication. Each man's estimation might be just as legitimate as ours. I think it is particularly dangerous to base our procedure on anything except purely medical necessities.

I am quite willing to admit at the present time that under some circumstances compromise may be necessary, but it must be recognized as a compromise and the compromise eliminated as promptly as possible and the profession should aim toward the ideal where such compromise will not be necessary.

DR. WILLIAM E. STUDDIFORD.—Are you speaking of the possibility of such a case being heard by a board on which you have representative sociologists, economists and a doctor?

DR. COSGROVE.—I was not thinking too specifically of that. Public funds can be used to avert starvation, as they are being used in this country and have been

used for the past decade or longer; those funds could similarly and just as legitimately be used for the alleviation of the socio-economic conditions which you and Dr. Watson speak of.

DR. STUDDIFORD.—If we are to absolve ourselves from such conditions I think we must have other people decide them for us.

DR. ROBERT L. DICKINSON.—Do we not in every medical condition take the economic conditions into consideration? In every other thing we are asked to do so. In abortion we throw them out.

DR. COSGROVE.—I don't know that that is very largely so, Dr. Dickinson. Pneumonia, for example, has to be treated properly. It is too bad if money stands in the way of that treatment, and in anything approaching a decent society, money should not be permitted to stand in the way of it.

Dr. Studdiford spoke of fixed hypertension and nephritis. I think my paper indicated that if there is any legitimate indication for therapeutic abortion it is in that type of case. However, if prolonged medical treatment and hospitalization were applied to all of those, certainly the number that would have to be aborted would be tremendously reduced.

Dr. Kosmak says I should not talk of murder. I diametrically disagree with him on that. I acknowledge the possibility of justifiable murder as I clearly enough outlined in my paper. If I admit the occasional justification of murder, certainly he should not balk too much at my calling abortion what it actually is, murder, premeditated destruction of human life.

Dr. Taylor's is a legitimate question, and I am frank to say, I cannot answer it. There have been occasional cases which, on review, I would concede had been better aborted. I believe that those cases are very rare; however, I have not searched our records for material with which to specifically answer that question.

I am surprised, however, to hear Dr. Loizeaux say that the decision in cardiac cases is up to the cardiologist. On my service, it is understood that the obstetrician should not be a mere mechanic to carry out the direction of a specialist in another field; he has the same right that any practitioner has to seek consultation, and then to evaluate that counsel in his own judgment and make the final decision himself. I think there is altogether too great a disposition for the obstetrician to merely carry out the orders of this or the other specialist.

DR. LEON S. LOIZEAUX.—We have to have the opinion of a ranking man in that department. We have difficulty in arguing about those cases if they come to us with a recommendation from the specialist. Sometimes it is obvious that they are right, and sometimes it is obvious that we are wrong.

DR. COSGROVE (closing).—I think Dr. Burns' report of a death from hyperemesis antedated the more modern treatment and that he would not have lost that patient today.

I am glad Dr. Heaton appreciated that some of the discussers seemed to miss the whole point of the paper and he properly questions by what authority a standard for our guidance shall be erected. I have argued tonight as the whole point of what I have been trying to say that we should not depend on legal or religious or any other authority; that we ourselves, on the basis of our own conscience evolve our own standards, and be our own authority for the standards that we seek to follow.

THE RELATION OF BASAL METABOLIC GAIN DURING PREGNANCY TO NONPREGNANT BASAL METABOLISM

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STUDIES of basal metabolism during normal pregnancy have clearly shown that a rise occurs during the late months of pregnancy. This rise generally averages around 15 per cent.¹⁻³ Yet there is a great deal of individual variation. Some women have a basal gain of 30 per cent or more during gestation while others show an actual decline in rate. Aside from possible experimental errors, there are probably many factors which might influence the degree of rise. An individual developing a hydramnios would not be expected to show an increase of oxygen consumption commensurate with her weight increase. Edema increases weight without a corresponding increase in oxygen need. Patients who acquire excessive adipose tissue during pregnancy might perhaps show a lesser percentage rise in basal metabolism. Richards and Newberry⁴ have shown that women with more active fetuses have greater increases in basal rate, perhaps due directly to oxygen needs of their energetic fetuses. Small women with large fetuses should have large rises. One factor of possible importance in determining the degree of pregnancy rise might be the state of function of the thyroid gland during nonpregnancy. We shall present here a study of the relationship between pregnancy basal rise and nonpregnant basal level. Our question is, do women with low nonpregnant basals show a large, a small, or an average rise during gestation?

Methods and Results

At the Fels Research Institute, we have had under careful observation nearly two hundred pregnant women.⁵ A part of our observation has consisted of basal metabolic rate determinations, at the end of each trimester, or at monthly intervals, and twelve months postnatally. The indirect method was used. The frequency of the tests insured absence of apprehension and good cooperation. All tests were done in duplicate, and the lower of the two results was used, unless there was obvious reason to believe it inaccurate. The normal standards used in calculating results were those of Boothby, Berkson and Dunn.⁶ The research subjects were all "normal" women selected upon the basis of their willingness to cooperate, but without regard to previous basal rate. Basal gain was calculated by subtracting post-partum rate from ninth month rate. From the entire group we eliminated: (1) Those patients upon whom either ninth month or a post-partum basal was not available; (2) those with severe dyspnea or other difficulty, whose tests were technically unsatisfactory; (3) those with toxemia or other systemic

condition which might affect basal rate; (4) those with toxic goitre. Data on the remaining 158 women constitute the material for this study.

The correlation coefficient (Pearsonian) between pregnancy basal gain and nonpregnant basals is $-.62$. From this figure it is evident that in our group those women who had the lowest nonpregnant basal metabolic rates tended to have the greatest pregnancy gain. This correlation coefficient is great enough to be highly significant. Yet the

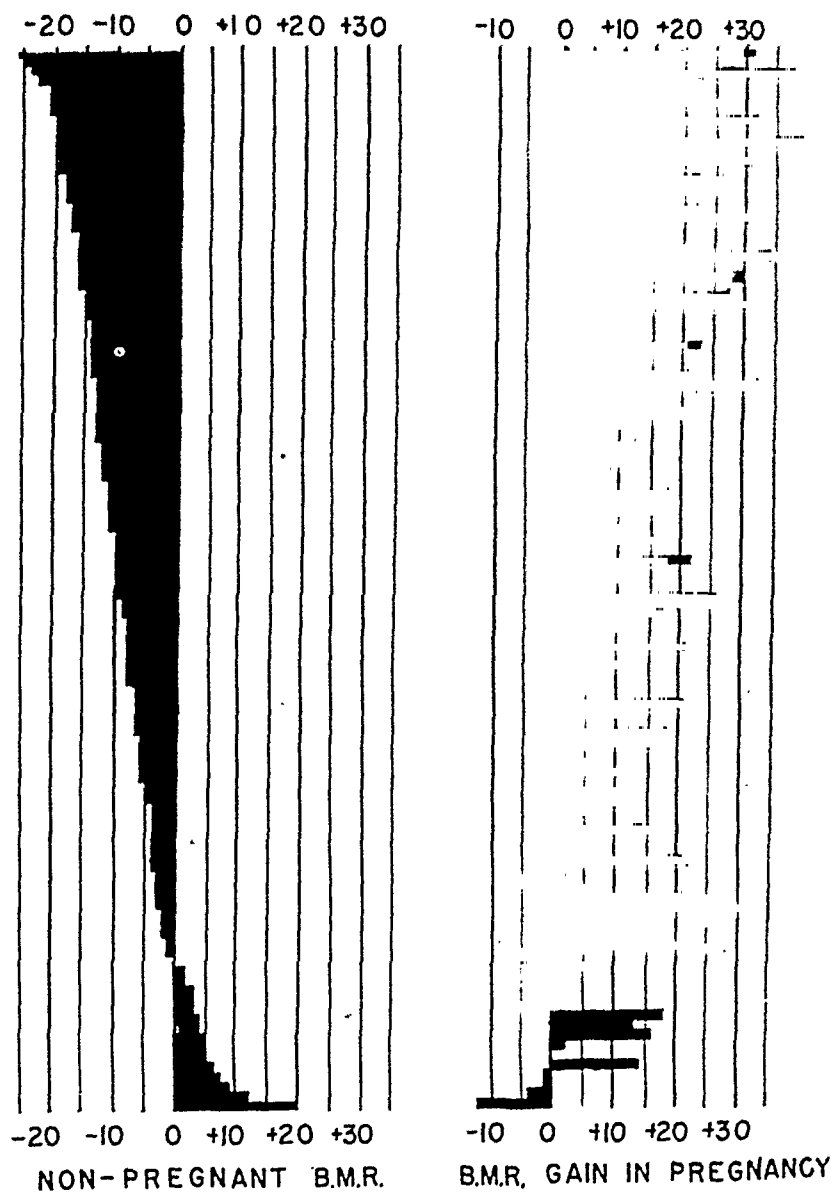


Fig. 1.

fact that it is not -1.0 indicates there are exceptions to the relationship it expresses. Fig. 1 shows the relationship graphically. From this figure it is evident that the preponderance of high basal gains occurred among the women with the lowest nonpregnant basals, but that there are several exceptions.

Table I contains the means and standard deviations of nonpregnant, ninth month pregnant, and pregnancy gains in Basal Metabolic Rate for our group.

TABLE I

| B.M.R. CLASSIFICATION | NO. | MEAN | STANDARD DEVIATION |
|------------------------------------|-----|-------|-----------------------|
| Nonpregnant B.M.R. | 115 | -8.33 | 9.7 |
| B.M.R. in ninth month of pregnancy | 158 | +5.89 | 8.5 |
| B.M.R. gain during pregnancy | 142 | 14.27 | 10.8 |

Table II shows the distribution of values for nonpregnant and ninth month pregnant basals and basal gains during pregnancy.

TABLE II. DISTRIBUTION OF VALUES FOR THREE B.M.R. CLASSIFICATIONS IN THE FELS INSTITUTE SERIES

| PER CENT | NONPREGNANT | | NINTH MONTH | | PREGNANCY GAIN | |
|----------------|-------------|----------|-------------|----------|----------------|----------|
| | NO. | PER CENT | NO. | PER CENT | NO. | PER CENT |
| Plus 36 to 40 | | | | | 2 | 1.9 |
| Plus 31 to 35 | | | | | 8 | 7.5 |
| Plus 26 to 30 | | | 2 | 1.9 | 7 | 6.5 |
| Plus 21 to 25 | | | 1 | 0.9 | 14 | 13.1 |
| Plus 16 to 20 | 1 | 0.9 | 9 | 8.4 | 19 | 17.8 |
| Plus 11 to 15 | 1 | 0.9 | 16 | 15.0 | 21 | 19.6 |
| Plus 6 to 10 | 3 | 2.8 | 22 | 20.6 | 11 | 10.3 |
| Plus 1 to 5 | 10 | 9.3 | 25 | 23.4 | 12 | 11.2 |
| 0 | 1 | 0.9 | 8 | 7.5 | 1 | 0.9 |
| Minus 1 to 5 | 18 | 16.8 | 18 | 16.8 | 9 | 8.4 |
| Minus 6 to 10 | 25 | 23.4 | 5 | 4.7 | 2 | 1.9 |
| Minus 11 to 15 | 23 | 21.5 | 1 | 0.9 | 1 | 0.9 |
| Minus 16 to 20 | 18 | 16.8 | | | | |
| Minus 21 to 25 | 6 | 5.6 | | | | |
| Minus 26 to 30 | 1 | 0.9 | | | | |

Our values for basal gain correspond very closely with those of other investigators.^{1, 2} Our nonpregnant basal values are low on the basis of the Boothby, Berkson and Dunn standards. Davis⁷ has published a study of basal metabolism determinations on pregnant and nonpregnant women in Milwaukee, Wisconsin, and Wilmington, Delaware. His mean values are also notably below the standards he used, presumably again the Boothby, Berkson and Dunn standards. A comparison of his figures with ours (Table III) shows that our values for nonpregnant basals are even lower than those of his Milwaukee group.

TABLE III. A COMPARISON OF NONPREGNANT B.M.R. DISTRIBUTION IN THE FELS SERIES WITH THE MILWAUKEE AND WILMINGTON WOMEN STUDIED BY DAVIS

| | B.M.R. ABOVE PLUS 10% | B.M.R. IN NORMAL RANGE | B.M.R. BELOW MINUS 10% |
|---------------------------|--------------------------|---------------------------|---------------------------|
| Fels nonpregnant series | 1.8% | 53.4% | 44.8% |
| Milwaukee series (Davis) | 16.7% | 52.4% | 30.9% |
| Wilmington series (Davis) | 5.5% | 50.0% | 44.5% |

Boothby, Berkson, and Dunn, in presenting their norms for basal metabolic rate, very carefully explain that their figures are derived from tests on Mayo Clinic cases. They are done without benefit of practice. Since the metabolism tests were a part of the total diagnostic procedure of the Clinic and were done on medical patients seeking diagnosis and treatment, they may have been influenced by an element of anxiety. Since the environment and circumstances surrounding the testing of Davis' patients and also our series were very different, and since in both series there was a good deal of practice, we may perhaps

assume that these elements are responsible for a considerable degree of the difference between the Mayo series and Davis and ours.

Table IV compares Davis' late pregnancy basals with our ninth month basals.

TABLE IV. A COMPARISON OF NINTH-MONTH B.M.R. DISTRIBUTION IN THE FELS SERIES WITH THE WILMINGTON LATE PREGNANCY GROUP STUDIED BY DAVIS

| | B.M.R. ABOVE PLUS 10% | B.M.R. IN NORMAL RANGE | B.M.R. BELOW MINUS 10% |
|---|--------------------------|---------------------------|---------------------------|
| Fels ninth month pregnancy series | 26.2% | 72.9% | 0.9% |
| Wilmington late pregnancy series (Davis) | 6.0% | 62.0% | 32.0% |

Despite the fact that our nonpregnant group has basals comparable to Davis' Wilmington group, our ninth month group has a higher mean basal rate than Davis' late pregnancy group. Perhaps this fact may be accounted for his inclusion of seventh and eighth month basals in his late pregnancy group, whereas our tests are all made during the ninth month.

The degree of difference between Davis' and our nonpregnant basals and those which comprise the Mayo Clinic standards suggests at once the need for interpreting the results of any basal metabolic test in terms of the conditions under which it was made. It is probably not justifiable to assume that because our basals or those of Davis are lower than those of the Mayo Clinic group, that hypothyroidism is more highly prevalent in Milwaukee, Southern Ohio or Delaware, although of course such might be the case. It seems more reasonable to assume that since the women upon whom we made our tests were people who had been collaborating for periods of months or years in our research program here, since they did not come for diagnosis but rather to undergo a routine part of our research procedure, and since in most instances they had had considerable opportunity for practice in the recording of a basal metabolic rate, that they suffered from a minimum degree of apprehension. Their complete familiarity with the technique and their lack of apprehension about themselves and what the results of the test might yield, give a more nearly basal set of values than are represented in the Mayo Clinic group. From basals taken under such conditions, we should perhaps be very hesitant in interpreting a basal result of minus 15 or minus 20 on the basis of the Mayo standards, as indicating hypothyroidism. For the average hospital or clinician, the Mayo standards are far more valid than any derived from data such as ours.

Discussion

There probably is some adequate physiologic explanation for the tendency shown in Fig. 1, for mothers with low nonpregnant basals to score the greatest gains in basal rate during pregnancy. Three possible explanations occur to us and are perhaps worth stating.

1. It is generally accepted that individuals with inadequate thyroid function are more sensitive to a small dosage of desiccated thyroid substance than are persons with normal thyroid function. It is usually easier to produce a rise in basal metabolic rate in a hypothyroid individual by thyroid therapy, than it is in a normal individual by the

same therapy. If then the fetal thyroid contributes an important share to the total fetal-maternal thyroid economy, the maternal system should respond with a greater increase in metabolic rate if a hypothyroidism existed than it should if that maternal system had a normally functioning thyroid. In other words, the fetal thyroid would correspond to more effective thyroid therapy if a hypothyroidism existed in the mother.

2. The fetal thyroid, like the fetal pancreas in a diabetic mother, may be capable of expanding its output to compensate for maternal deficiency and by so doing strive to produce a state of optimum maternal fetal thyroid function. Such a mechanism would permit a maternal system with low thyroid function to attain the same optimum state of metabolism as would occur with a normal maternal and average fetal thyroid.

3. It is possible that the physiologic changes of pregnancy provide a resurgence of function of the maternal thyroid. Thus, for the period of pregnancy, it may become a normally functioning gland and in doing so cause a greater than average basal gain over the nonpregnant state.

The exceptions to the low nonpregnant basal-high gain finding may involve many factors such as weight gain, size of the fetus, deviations in functions of the other glands, etc. For example, in our group there is a correlation coefficient of $+0.22$ between basal gain and weight of the fetus. This figure, while low, is significant at the .05 level of reliability. From this figure one may presume that a small fetus from any cause might be expected to influence toward a lower figure the mother's basal gain. More difficult to explain, however, are those not infrequent cases where an actual decline in basal rate occurs during pregnancy. In these instances, it is perhaps reasonable to assume that a less adequate food iodine intake in late pregnancy, lessened emotional stress, glandular or other factors were at the time of pregnancy in the process of lowering the metabolic level; or that some process during the period when the nonpregnant basal was taken had raised it above its "normal" level. Certainly if the pregnancy drop had been due to failure of development of the fetal thyroid, the child from such a pregnancy would have been cretinous, and such was never the case in our series.

Summary

The relationship between the nonpregnant basal metabolic level and the basal metabolic gain during pregnancy was investigated in 158 women of the Fels Research Institute series.

Women who had the lowest nonpregnant basal metabolic rates tended to have the greatest pregnancy gains. Possible explanations of this finding, as well as a discussion of the exceptions which occur, are presented.

In the Fels nonpregnant series, 44.8 per cent of the women had basal metabolic rates below -10 per cent on the basis of the Mayo Clinic

standards. Basal metabolic rates during the ninth month of pregnancy were preponderantly at the level which would usually be considered normal for nonpregnant women. These facts can probably be explained on the basis of differences in the conditions under which various basals are measured.

The low basal metabolic rates observed in the Fels series were compared with Davis' Milwaukee and Wilmington series, which also showed low values. The possible need for interpretation of test results in terms of the environment, significance the patient attaches to the test, general anxiety, and previous test experience is suggested.

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MEASUREMENT OF THE CYCLIC VARIATIONS IN THE QUANTITY OF CERVICAL MUCUS AND ITS CORRELATION WITH BASAL TEMPERATURE*

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SÉGUY and Vimeux¹ were among the first to report cyclic changes in the amount of cervical mucus in normally menstruating women. They found that the amount of mucus is greatly increased from about the tenth to the fifteenth day after the beginning of the last menstrual period. At this time the mucus is glairy, transparent, and relatively acellular. In a later paper Séguy and Simonnet² correlated this phenomenon with an increase in urinary folliculin and with visual evidence of ovulation by inspection of the ovaries at laparotomy.

Lamar, Shettles and Delfs³ confirmed and extended these observations. In addition to studies on the amount and viscosity of the cervical mucus, they found that spermatozoa can penetrate the mucus to an appreciable distance only during this period of increased secretion and during menstruation.

Basal body temperature curves have been used for estimating the time of ovulation. Reviews of the literature on this subject can be found in the reports by Barton⁴ and Lyon.⁵ According to current interpretations the vaginal temperature is maintained at a relatively low level during the follicular phase of the cycle, rises abruptly following ovulation and remains at this higher level throughout the progestational phase of the cycle. The temperature drops with the onset of the next menses or within a day or two preceding the actual onset of bleeding. Ovulation is considered to have occurred between the time of the last low and the first high temperature. Women having anovulatory cycles, castrates, children and men do not show these biphasic curves.

Various investigators have correlated basal body temperature with other signs of ovulation such as electric potential shifts,⁴ endometrial biopsies,⁶ basal metabolic rates,⁷⁻⁹ sodium pregnanediol glucuronidate, gonadotropin and estrogen excretions,¹⁰ and vaginal smears.^{7, 10-11}

The amounts of mucus present in the cervix as reported in the literature have been estimated by the observers merely as small, moderate, or large. It has been felt by the present authors that a more objective measurement might be of value and to that end the following data have been obtained. Since the basal body temperature shift is believed by many to be a fairly reliable method for fixing the time of ovulation,

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it was thought that a study of the time relationship between basal temperature changes and the quantity of cervical mucus might prove interesting.

Material and Methods

A dry speculum was inserted to expose the cervix. If the vaginal secretion grossly contaminated the cervical mucus at the external os, an attempt was made to wipe it away with a cotton swab. This usually resulted in a slight loss of cervical mucus due to the tenacity of the latter. It was necessary to follow this procedure only occasionally.

A weighed glass cannula was then inserted a few millimeters into the external os and the mucus was withdrawn by aspiration with an attached 20 c.c. syringe. An attempt was made to evacuate the canal completely, using a second cannula if necessary. The cannulae were again weighed and the amount of mucus was determined by difference.

Daily temperatures were taken vaginally in the morning before arising using a clinical thermometer graduated to 0.2 of a degree Fahrenheit. The thermometer was left in place for five minutes before taking the reading and subjects were instructed to estimate the temperature to the nearest 0.1 of a degree.

Four nulliparous married women were used as subjects.

SUBJECT 1.—Aged 25, was followed through six consecutive cycles which were 27, 25, 26, 27, 25 and 27 days long respectively. The menstrual history and physical examination were normal. Except on Sundays and holidays, she was examined daily between 9 and 10 A.M. In a number of instances during the first four cycles, she was examined again at about 12 o'clock, or between 3 and 4 P.M. During cycles 5 and 6 single daily mucous specimens were obtained. During the first four cycles, the subject used a diaphragm as a contraceptive followed by a douche the next morning. No contraceptives were used in the last two cycles but a douche was taken the morning following intercourse.

In some instances even 8 or 9 hours after a douche, the material obtained by aspiration was abundant in amount, quite transparent, and of low viscosity regardless of the day of the menstrual cycle. When seen again the following day at the usual time, the findings were again those representative of the period in the cycle. In other instances, the use of a douche did not seem to alter the amount and characteristics of the mucus to be expected for that particular day of the cycle, but to avoid introducing any variable error, all specimens obtained on days when a douche was taken are excluded from the data.

SUBJECT 2.—Aged 26, was followed through three nonconsecutive cycles of 26, 27 and 27 days respectively. The menstrual history and physical examination were normal. Mucous specimens were obtained once daily except on Sundays and holidays with the exception of the second cycle when the subject was ill with a minor intestinal disorder during days 13 through 18. Oral temperatures taken on these days were normal so the vaginal temperature curve also has been considered normal. As a contraceptive, the subject used a diaphragm followed by a douche the next morning. For the same reasons as discussed under Subject 1, specimens obtained on these days are not included in this report.

SUBJECT 3.—Aged 20, was followed for one complete cycle of 27 days. In the next two cycles because of mild upper respiratory infections only a few scattered observations were made. The menstrual history and physical examination were normal. This subject also used a diaphragm

as a contraceptive and followed this by a douche the next morning. The same procedure was carried out with her as with Subjects 1 and 2.

SUBJECT 4.—Aged 25, was followed through three consecutive cycles. The first two were 34 and 29 days long, respectively, and pregnancy occurred in the third cycle. The menstrual history and physical examination were normal. This subject was anxious to become pregnant and used no contraceptives at any time. Inasmuch as the effect of the semen

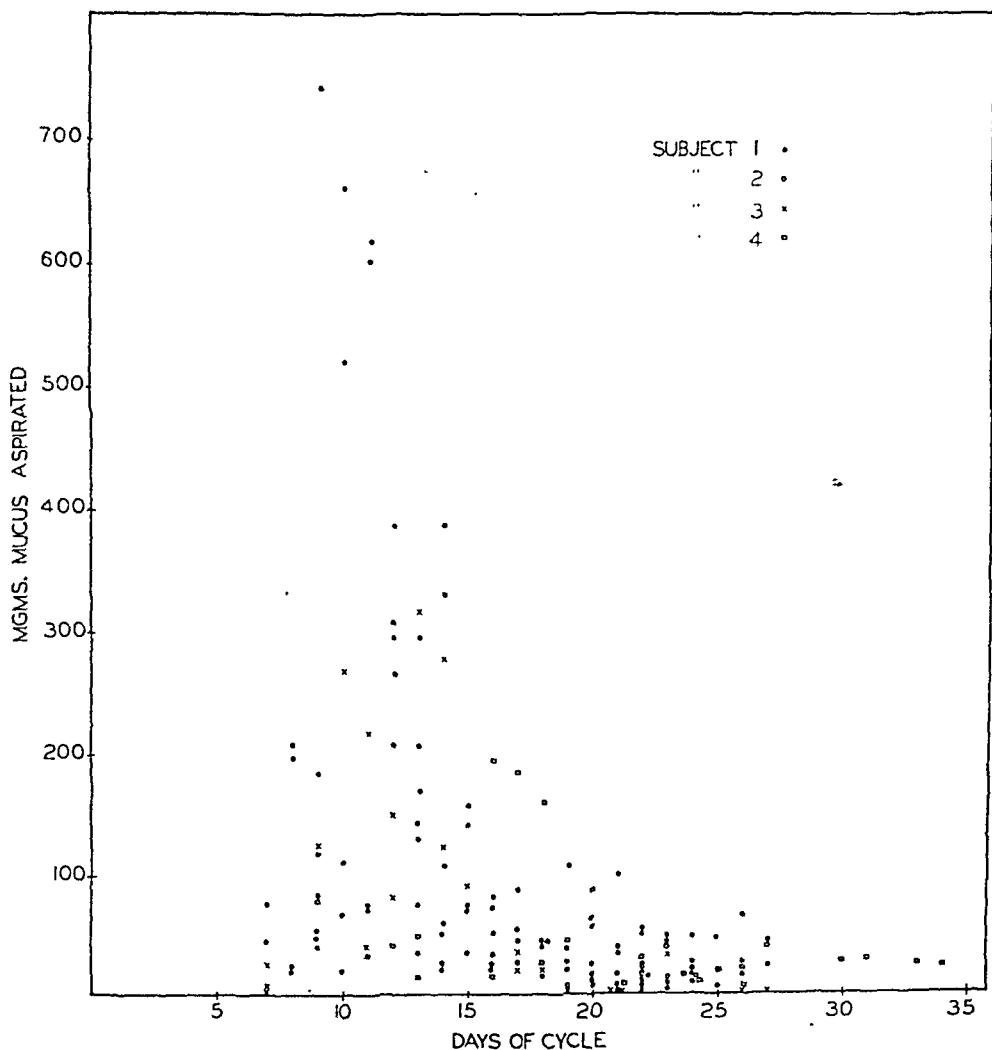


Fig. 1.—Relation between the amount of cervical mucus and the time in the menstrual cycle. One hundred fifty-one observations in 14 cycles of 4 individuals.

on the cervical mucus might very probably introduce a variable error in the consideration of normal values, specimens obtained on the days following intercourse were not included. For this reason very little data were obtained from about the fifteenth through the twentieth days of the cycles. Data obtained after the twentieth day of cycle 3 are not included because of pregnancy.

Results

The amounts of cervical mucus obtained throughout all the menstrual cycles of the four subjects are shown in Fig. 1. A total of 151 observations were made, 72 for Subject 1, 30 for Subject 2, 23 for

Subject 3, and 26 for Subject 4. It can be seen that the amount of mucus is increased from about the eighth through the eighteenth days considering the group as a whole. If the individuals are considered separately, the peaks are from the eighth through the thirteenth days for Subject 1, the twelfth through the fifteenth days for Subject 2, the tenth through the fifteenth days for Subject 3, and the sixteenth through the eighteenth days for Subject 4. The reason for a later peak in this case is readily explainable on the basis of her longer cycles.

In general, there seems to be a level of about 60 mg. or less, both preceding and following the days of increased secretion. The greatest amount of mucus, 741 mg. in a single observation, was obtained in Subject 1. This is about a twelvefold increase over the secretion at other times in the cycle. This subject consistently secreted more mucus during the peak than any of the others. In the other individuals the maximum amount varied from about 200 to 400 mg.

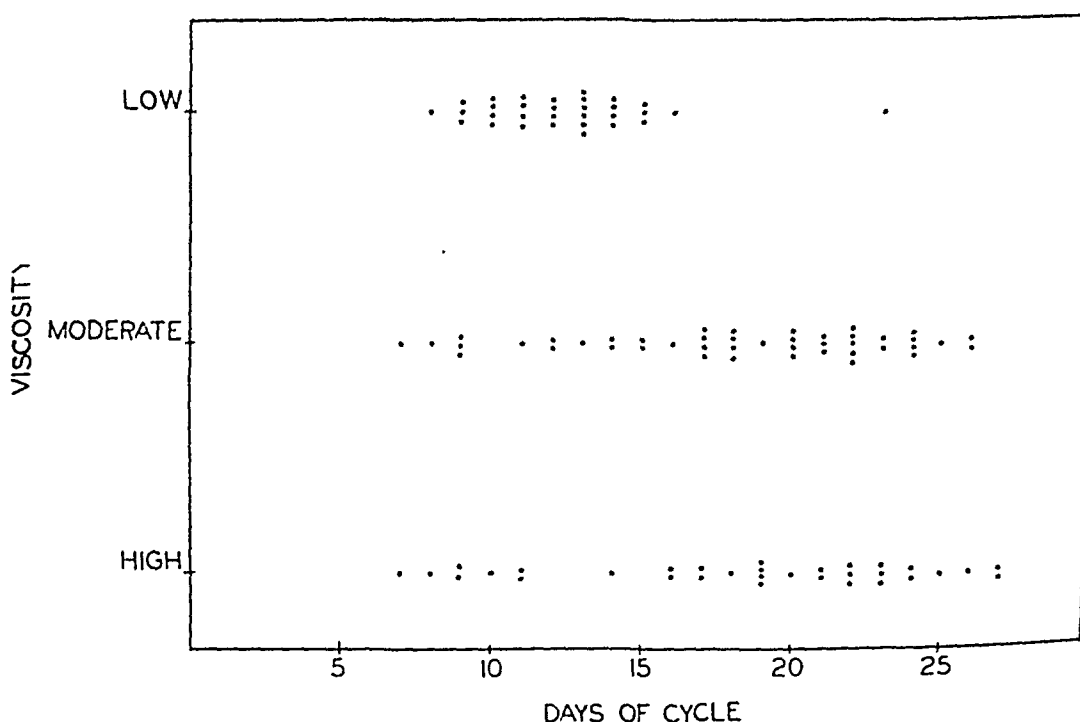


Fig. 2.—Relation between the viscosity of cervical mucus and the time in the menstrual cycle. One hundred seven observations in 10 cycles of 4 individuals.

Subjects 1 and 4 were aspirated twice daily during part of this study; the first aspirations were made at 9 A.M. and the second at about 12 noon, or at 3 to 4 P.M. Typical findings are shown in Table I. In 52 out of a total of 59 instances the second aspiration, whether made at noon or later yielded a slight but significantly greater amount of mucus than the first. In two instances, the amount was the same at both aspirations, and in five instances, the second aspiration yielded less than the first. There are several possible explanations for this phenomenon. One is that during the night when the individual is at rest, less mucus may be produced. Coincident with increased bodily activity upon arising, the rate of secretion may be increased. Another possibility is that, since the individual has been lying in a horizontal position for some 8 or 10 hours, the mucus may have accumulated at the uterine end of the cervical canal. It might be that a vertical position after arising may

facilitate drainage of the mucus which has been retained. Since the first aspirations were made approximately two hours after arising and the second some five or more hours after arising, more of the mucus might reach the external os later in the day. This problem is being studied in greater detail at the present time.

No objective method for measuring the viscosity of cervical mucus has as yet been found. During the course of this work it has been estimated as high, moderate or low by observing the ease with which the mucus could be drawn up into a small glass capillary of approximately 0.4 mm. inside diameter. The results of 107 observations in 10 cycles are shown in Fig. 2. The viscosity is usually low from the eighth through the sixteenth days of the cycle if the group is considered as a whole. The range of low viscosity for any one cycle is usually only 4 or 5 days. Only at one observation was a low viscosity encountered after the sixteenth day, namely on the twenty-third day. The reason for this atypical instance is not known. Our results are in general accord with those obtained by Lamar et al.³

TABLE I. THE AMOUNTS OF CERVICAL MUCUS OBTAINED WHEN CERVIX IS ASPIRATED TWICE DAILY

| DAY OF CYCLE | FIRST ASPIRATION | SECOND ASPIRATION | |
|--------------|---------------------|-------------------|--------------------|
| | 9 TO 10 A.M. MG. | 12 NOON MG. | 3 TO 4 P.M. MG. |
| 8 | 53 | 71 | |
| 9 | 41 | 67 | |
| 10 | 272 | 389 | |
| 12 | 201 | | 185 |
| 13 | 86 | | 58 |
| 14 | 47 | | 62 |
| 15 | 38 | | 104 |
| 16 | 43 | | 40 |
| 17 | 29 | 59 | |
| 19 | 19 | 49 | |
| 20 | 14 | 45 | |
| 21 | 16 | 42 | |
| 22 | 13 | 24 | |
| 23 | 10 | 40 | |
| 24 | 20 | 33 | |
| 26 | 33 | | 36 |
| 27 | 10 | | 34 |

Basal vaginal temperatures were recorded and correlated with the amount of cervical mucus through a total of 7 cycles. In order to best illustrate these observations, the results are shown by individual cycles in Fig. 3. Correlations between temperature and the amount of cervical mucus were studied in cycles 3 through 6 in Subject 1. Using the temperature shift as the criterion, ovulation presumably occurred between the thirteenth and fourteenth days in cycles 3 and 4, and between the twelfth and thirteenth days in cycles 5 and 6. In each cycle the maximum secretion of cervical mucus preceded the temperature rise by at least one day, and in one instance, cycle 5, by three days. Penetrability studies done in cycles 3 and 4 according to the method of Lamar et al.³ indicated that the optimum conditions for penetration of the cervical mucus by spermatozoa existed days 11 through 13. Coitus without contraceptives on the fourteenth day of cycle 6 did not result in pregnancy. The patient reported in a follow-up visit that in the next succeeding cycle coitus on the thirteenth and fourteenth days did not result in pregnancy either. While repeated exposures often

transpire before pregnancy results, it is interesting to speculate whether for this particular individual impregnation would be more probable if intercourse had taken place on days 11 and 12 when the optimal conditions for impregnation may have existed.

Data from three noneconsecutive cycles are available for Subject 2. Because of illness in cycle 2, as mentioned previously, it was not possible to correlate the temperature with the amount of mucus. In cycle 1, the subject experienced definite midmenstrual pain in the afternoon and evening of the thirteenth day. The temperature on the fourteenth day was 1.9 degrees higher than the low on the preceding day. The temperature did not remain this high but fell to a level averaging 0.7

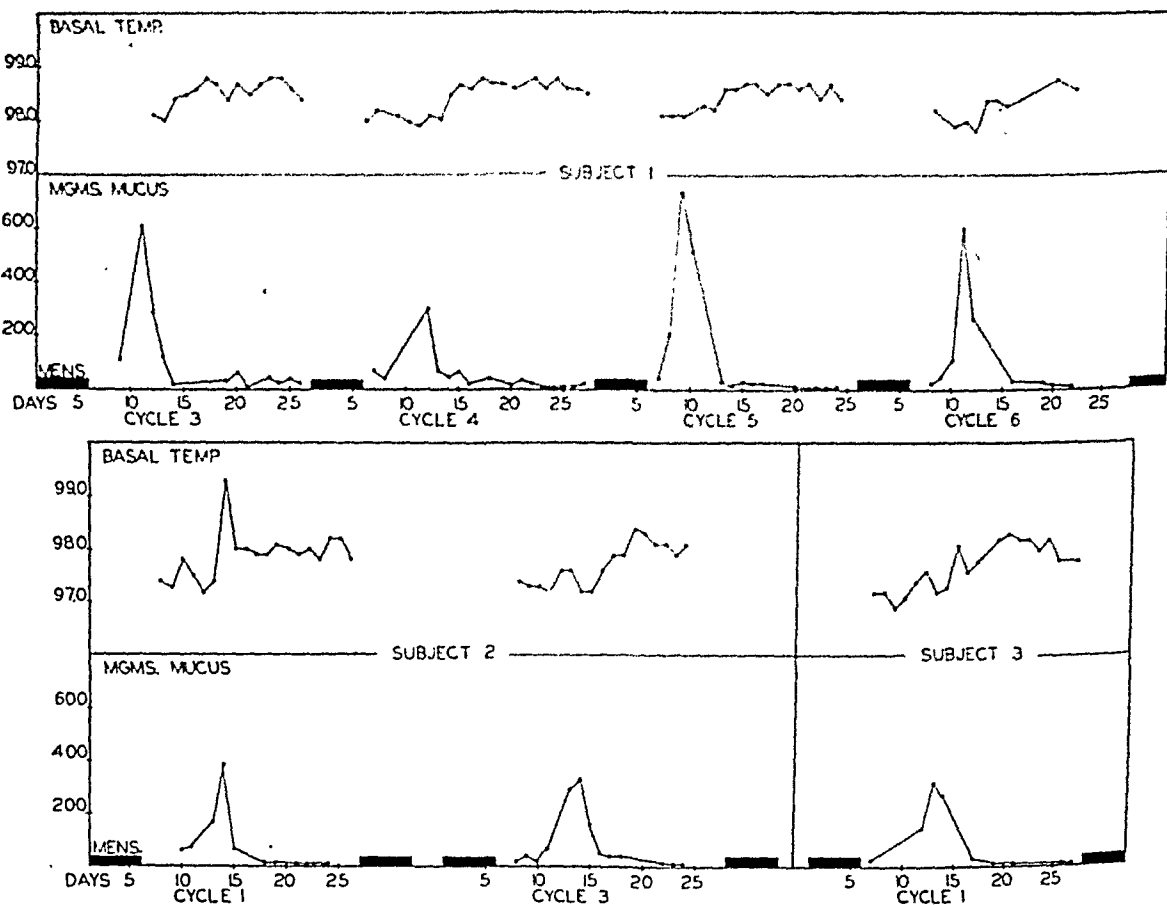


Fig. 3.—Relation between the amount of cervical mucus and the basal temperature. Seven cycles of 3 individuals.

degrees higher than the prethermal shift average. The maximum secretion of mucus coincided with the time of the temperature rise, i.e., on the fourteenth day. The amounts of mucus on days 13 and 15 were 200 to 300 mg., less than the peak of about 400 mg., certainly a significant difference. This is the only cycle of the seven studied in which the temperature shift and maximum secretion of mucus occurred on the same day.

In cycle 2, where only the temperature record is available, midmenstrual pain again occurred on the thirteenth day. On the fourteenth day, the temperature reached a peak of 99.1 degrees, a rise of 1.7 degrees.

In cycle 3, no midmenstrual pain was experienced and no significant peak was obtained in the temperature record, although a moderate rise

was observed. Ovulation presumably occurred between the fifteenth and sixteenth days, while the maximum secretion occurred on the thirteenth and fourteenth days. Here, as in Subject 1, the maximum secretion preceded the temperature rise. This individual used contraceptives throughout the cycle so no data are available concerning the possibility of impregnation.

In Subject 3, correlation between temperature shift and the amount of cervical mucus was obtained in one cycle. The temperature shift came between the fourteenth and fifteenth days, and the maximum secretion of cervical mucus was from the twelfth through the fourteenth day, with the peak on the thirteenth. Here again, the maximum secretion occurred shortly before the temperature shift.

In Subject 4, temperatures were recorded only during the last cycle, i.e., the one which terminated in pregnancy. The temperature rise came between the sixteenth and seventeenth days which correlates well with the fact that her cycles were 29 to 34 days long. No specimens of mucus uncontaminated by semen were available for days 15 through 18 but the amounts aspirated during these days were definitely larger than those obtained under similar circumstances during the latter half of the cycle. This would seem to indicate that the maximum secretion probably occurred during those days.

The vaginal temperatures for this subject remained high beyond the date of the expected menses, and a Friedman test done on the thirty-fourth day after the beginning of the last menstrual period was positive. The pregnancy has since been confirmed clinically. This persistence of an elevated basal temperature beyond the date of the anticipated menses, i.e., in early pregnancy, is in accord with the findings of others.¹¹⁻¹⁴

Vaginal smears and smears of cervical mucus taken daily and stained by the method of Shorr¹⁵ were studied in this laboratory, but we were unable to discern from them definite changes that could be correlated with the exact time of ovulation.

Discussion

Our results are in agreement with those of Séguy and Vimeux¹ and of Lamar, Shettles and Delfs³ that cervical mucus undergoes cyclic variations in amount. In addition, we have weighed the mucus obtained by aspiration instead of estimating it subjectively. The amounts of cervical mucus we have aspirated do not represent the total secretion per 24 hours. However, the subjects were seen at approximately the same time each day so we feel that the variations between aspirations are significant.

From the small series of cycles presented here showing the time relationship between the amount of cervical mucus and the basal temperature, it is evident that in these normal individuals the maximum secretion of cervical mucus usually precedes the temperature rise. This may be the explanation for the fact that in Zuck's series¹² some individuals having coitus after the temperature rise failed to become pregnant.

A study covering the time relationship between the amount of cervical mucus, the basal temperature, and planned pregnancies resulting

from single exposures would be highly interesting, but so far an adequate supply of clinical material has not been available.

A study of the cyclic variations in the amount of cervical mucus and their relation to basal temperature in cases of unexplained sterilities might be profitable. One such individual, who menstruates regularly and who has had the usual sterility investigation, was followed through four cycles. The temperature curves indicated that ovulation was probably not occurring. The cervical mucus increased in amount near the expected time but the viscosity remained high. The injection of estrogens did not lower the viscosity. Obviously the cause of the sterility is related to the failure to ovulate in this case.

We feel that by the procedures used in this study, the presence or absence of ovulation can be detected with as much accuracy as by endometrial biopsies or by prolonged hormone studies. There is no discomfort to the patient, the tedious procedure of collecting urine specimens is avoided, and no special equipment is needed.

Summary

1. The amount of cervical mucus that can be aspirated daily throughout the menstrual cycle has been measured quantitatively.

2. About 60 mg. or less is obtained from the end of the menstrual period to about the eighth or ninth day of the cycle. The amount then increases markedly for about 4 days. The peak of maximum secretion varies from about 200 to 700 mg., depending upon the individual observed. The secretion then falls abruptly to the previous level of 60 mg. or less, and remains there throughout the rest of the cycle.

3. In six of seven cycles where the time relationship between the amount of cervical mucus and the basal temperature was observed, the maximum secretion preceded the rise in temperature by one to three days. In the seventh cycle, the maximum secretion and the temperature shift occurred on the same day.

4. It is suggested that similar studies be applied to cases of otherwise unexplained sterility.

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THE MANAGEMENT OF DELIVERY IN PREGNANCY COMPLICATED BY SERIOUS RHEUMATIC HEART DISEASE

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MANY obstetrical institutions consider cesarean section the safest method of delivery in pregnancy complicated by serious rheumatic heart disease. Several authors have recently commented upon the high maternal mortality following cesarean section performed because of heart disease, and have questioned the indication in such poor surgical risks. Gorenberg and McGeary¹ report a mortality of 6.9 per cent following abdominal delivery as compared to 1.2 per cent following vaginal delivery. Gorenberg² states that heart disease is no indication for cesarean section. Greenhill³ claims that there is practically no necessity to resort to cesarean section when the sole indication is rheumatic heart disease. Hamilton and Thomson⁴ report mortalities of 8.3 per cent and 2.3 per cent, respectively, for abdominal and vaginal deliveries. They also find a higher incidence of cardiac failure, embolism and sepsis following abdominal delivery. However, none of the above authors has presented acceptedly similar vaginal and abdominal groups to warrant comparison of methods of delivery.

The trend toward cesarean section for rheumatic heart disease was, in part, a reaction to the high mortality noted when cardiac patients were induced into premature labor with the expectation of obviating further increase in the circulatory burden. In the light of more recent knowledge, spontaneous improvement toward term is now anticipated, and such interference is generally contraindicated. The trend to cesarean section was also due to lack of criteria for evaluating the heart during labor.

In previous studies we attempted to find a practical method of evaluating the intrapartum cardiac status. In a series of normal women,⁵ it was observed that the pulse and respiratory rates remained practically unchanged throughout the first stage of labor. Certain increases in these rates were noted with the advent of bearing-down efforts in the second stage.

Two hundred cases of pregnancy complicated by rheumatic heart disease were next studied.⁶ The ante-partum functional capacity diagnoses according to the New York Heart Association criteria were: 72 Class 1, 109 Class 2, 17 Class 3, and 2 Class 4. One patient was delivered by cesarean section and the remainder were delivered vaginally. There were no deaths in the entire series. Intrapartum or post-

partum cardiac failure occurred in 3 per cent of the two hundred cases, none of whom had ever previously decompensated. Elevation of the pulse rate above 110 with elevation of the respiratory rate above 24, or such elevation of the pulse rate alone during the first stage of labor preceded each instance of cardiac failure by sufficient time to afford ample warning of its approach. No instance of cardiac failure occurred in patients with pulse and respirations below these critical levels during the first stage of labor regardless of the severity of the cardiac condition as indicated by the ante-partum functional classification. Rises in pulse and respiratory rates similar to those in normal women were observed during the second stage of labor but no serious significance could be attached to such rises unless they were preceded by similar first-stage values. We were particularly impressed with the outcome in bad cardias. Stress was laid upon good ante-partum care, functional evaluation, observation of the pulse and respiratory rates intrapartum, adequate digitalization and shortening of the second stage of labor. If similar results were obtained in a larger series, labor would be less formidable.

Present Study

There have been 41,459 pregnancies at the New York Lying-in Hospital from 1932 through 1943. Table I shows that pregnancy was complicated by rheumatic heart disease in 1,089 cases or 2.6 per cent. Table II shows the functional capacity distribution of cases according to the New York Heart Association criteria. The present study was undertaken primarily to evaluate the methods of delivery in serious rheumatic heart disease (Class 3 and Class 4). Table III shows there were eleven deaths in the 1,089 patients giving a total mortality of 1 per cent, but only eight or 0.7 per cent were due to the heart condition. These eight cardiac deaths were described in Table IV; all were due to decompensation—five ante partum and three post partum. The five ante-partum deaths occurred at the following months of pregnancy: one at the fifth, one at the sixth, two at the seventh, and one at the ninth. Two patients had been discharged from the hospital following recovery from a previous episode of cardiac failure. The three post-partum deaths followed abdominal delivery—one after hysterotomy and two after cesarean section.

TABLE I. INCIDENCE OF PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE AT THE LYING-IN HOSPITAL

| | |
|---|--------|
| Pregnancies, 1932 to 1943 | 41,459 |
| Pregnancies, 1932 to 1943 with rheumatic heart disease | 1,089 |
| Incidence of pregnancy complicated by rheumatic heart disease | 2.6% |

TABLE II. FUNCTIONAL CAPACITY IN PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE

| |
|-----------------|
| Class 1—480—44% |
| Class 2—442—41% |
| Class 3—113—10% |
| Class 4—54—5% |

TABLE III. MATERNAL DEATHS IN RHEUMATIC HEART DISEASE

| | |
|--------------------------|---------|
| Deaths in 1,089 patients | 11—1.0% |
| Cardiac deaths | 8—0.7% |
| Other deaths | 3—0.3% |

TABLE IV. CARDIAC DEATHS IN PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE

| CASE | AGE | PAR- ITY | GRAV- IDITY | LESION | ANTE- PARTUM FUNC- TIONAL CLASSI- FICA- TION | CAR- DIAC EN- LARGI- MENT | REMARKS |
|------------------|-----|-------------|----------------|----------------|--|---------------------------------------|--|
| DIED UNDELIVERED | | | | | | | |
| 1 | 28 | 0 | 2 | MI. MS, AI | 3 | + | Death due to failure at fifth month |
| 2 | 35 | 0 | 1 | MI. MS | 3 | + | Death due to failure with bronchitis at sixth month |
| 3 | 23 | 0 | 1 | MI. MS | 3 | + | Failure at sixth month, discharged after recovery, death due to failure at term |
| 4 | 31 | 1 | 2 | MI. MS, AI, AS | 3 | + | Death due to failure at seventh month |
| 5 | 21 | 0 | 1 | MI. MS | 3 | + | Failure at fifth month, discharged after recovery, death due to failure at seventh month |
| DIED POST PARTUM | | | | | | | |
| 6 | 40 | 3 | 5 | MI. MS | 3 | + | Failure at fifth month, cesarean section with tubal ligation under drop ether at term, death first day due to failure |
| 7 | 25 | 0 | 1 | MI. MS | 3 | + | Failure at fifth month with auricular fibrillation, cesarean section with tubal ligation under drop ether at eighth month, death eleventh day due to failure after febrile course with bronchopneumonia |
| 8 | 38 | 1 | 2 | MI. MS | 3 | + | Failure at fifth month with auricular fibrillation, cesarean section with tubal ligation under local at sixth month, death twelfth day due to failure after afebrile course complicated by peripheral emboli |

Table V shows the three deaths not attributable to the heart condition. These patients had less serious heart disease according to the functional capacity (Class 1 or Class 2) and at no time did they show any evidence of cardiac failure. One died ante partum of nephritis with uremia, and two died post partum of severe hemorrhage.

Table VI shows the type of delivery according to functional capacity. Forty-five patients were delivered abdominally with three deaths as previously described giving a mortality of 6.7 per cent. One thousand thirty-eight patients were delivered vaginally with no deaths. A comparison of mortalities would be of little significance if only the most

TABLE V. NONCARDIAC DEATHS IN PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE

| CASE | AGE | PAR- ITY | GRAV- IDITY | LESION | ANTE- PARTUM FUNC- TIONAL CLASSI- FICA- TION | CAR- DIAC EX- LARGE- MENT | REMARKS |
|------------------|-----|-------------|----------------|--------|--|---------------------------------------|---|
| DIED UNDELIVERED | | | | | | | |
| 1 | 28 | 0 | 2 | MI. MS | 2 | 0 | Death due to nephritis with uremia at seventh month |
| DIED POST PARTUM | | | | | | | |
| 2 | 29 | 1 | 2 | MI. MS | 1-2 | 0 | Death 11 hours post partum due to shock from 1,300 c.c. hemorrhage following normal delivery under gas-oxygen-ether after 4-hour labor at term. Normal pulse and respiratory rates throughout labor, no evidence of cardiac failure |
| 3 | 32 | 0 | 1 | MI. MS | 1-2 | 0 | Death 2 hours post partum due to shock from 1,000 c.c. hemorrhage following difficult midforceps with cervical and sulcus lacerations. Prolonged labor 80 hours with normal pulse rate throughout and no evidence of cardiac failure. Gas-oxygen-ether for delivery |

TABLE VI. TYPE OF DELIVERY ACCORDING TO FUNCTIONAL CAPACITY

| | CASES DELIVERED | CLASS 1 | CLASS 2 | CLASS 3 | CLASS 4 |
|----------------------|--------------------|-----------|-----------|-----------|----------|
| | 1,083 | 480-44.0% | 441-41.0% | 113-10.0% | 49- 5.0% |
| ABDOMINAL | 45- 4% | | | | |
| Hysterotomy | 9 | 2- 0.4% | 2- 0.5% | 3- 2.7% | 2- 4.1% |
| Cesarean section | 36 | 5- 1.0% | 10- 2.3% | 8- 7.1% | 13-26.5% |
| VAGINAL | 1,038-96% | | | | |
| Spontaneous abortion | 50 | 24- 5.0% | 21- 4.8% | 5- 4.4% | 0-0 |
| Therapeutic abortion | 54 | 0-0 | 24- 5.3% | 30-26.5% | 0-0 |
| Viable delivery | 984 | 449-93.6% | 384-87.1% | 67-59.3% | 34-69.4% |

serious cardiacs were delivered abdominally. Further analysis will therefore be concentrated upon the Class 3 and Class 4 cases.

Table VII shows the indications for the forty-five abdominal deliveries. Nineteen cases were in Class 1 or Class 2, and operation was performed without fatalities for indications other than the heart condition. Twenty-six cases were in Class 3 or Class 4 and there were no indications for operation apart from the severity of the cardiac disease. The twenty-six cases consisting of five hysterotomies and twenty-one cesarean sections are completely analyzed in Table VIII. Table IX shows the yearly distribution of these cases. The three deaths in this group have already been described in Table IV. Only one of three patients with auricular fibrillation survived abdominal delivery. This patient was a forty-three-year old para iv, gravida v

TABLE VII. INDICATIONS FOR ABDOMINAL DELIVERY IN PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE

| | | |
|--|--|----|
| A—Abdominal delivery in Class 1 or Class 2 rheumatic heart disease performed for indications other than the cardiac condition | | 19 |
| contracted pelvis 5, elderly primigravida 3, previous vaginal plastic 2, nephritis 2, previous cesarean section 2, breech 1, cervical dystocia 1, chorea 1, relative sterility 1, advanced arthritis 1 | | |
| Deaths | | 0 |
| B—Abdominal delivery performed because of Class 3 or Class 4 rheumatic heart disease | | 26 |
| Deaths | | 3 |

TABLE VIII. ABDOMINAL DELIVERY BECAUSE OF CLASS 3 OR CLASS 4 RHEUMATIC HEART DISEASE

| | HYSTEROTOMY—5 | | CESAREAN SECTION—21 | |
|-------------------------------------|---------------|---------|---------------------|-----------|
| | CLASS 3 | CLASS 4 | CLASS 3 | CLASS 4 |
| Number of cases | 3 | 2 | 8 | 13 |
| Deaths | 0 | 1 | 0 | 2 |
| Auricular fibrillation | 0 | 1 | 0 | 2 |
| Cardiac enlargement MI. MS. | 3 | 2 | 8 | 13 |
| Cardiac enlargement MI. MS. AI. AS. | 0 | 0 | 1 | 1 |
| Cardiac enlargement MI. MS. AI. | 0 | 0 | 1 | 2 |
| Primipara | 1 | 0 | 4 | 6 |
| Multipara | 2 | 2 | 4 | 7 |
| Normal pelvis | 3 | 2 | 8 | 13 |
| Age 35 or over | 1 | 0 | 3 | 5 |
| Elderly primigravida | 0 | 0 | 1 | 1 |
| Adequate digitalis | 2 | 2 | 8 | 13 |
| General anesthesia | 3 | 1 | 4 | 10 |
| Local anesthesia | 0 | 1 | 4 | 3 |
| Elective classical operation | 3 | 2 | 8 | 13 |
| Post-partum hemorrhage | 0 | 0 | 0 | 0 |
| Tubal sterilization | 0 | 1 | 7 | 12 |
| Cardiac failure before pregnancy | 0 | 1 | 0 | 4 |
| Cardiac failure ante partum | | 1 | | 9 |
| and post partum | | 1 | | 2 |
| Month of ante-partum failure | 123456789 | | Month Cases | 123456789 |
| | 1 | | | 13122 |
| Cardiac failure intrapartum | 0 | | | 0 |
| Cardiac failure post partum | 0 | | | 0 |

TABLE IX. ABDOMINAL DELIVERY BECAUSE OF CLASS 3 OR CLASS 4 RHEUMATIC HEART DISEASE

| YEAR | TOTAL CASES | HYSTEROTOMY | CESAREAN |
|------|-------------|-------------|----------|
| 1932 | 18 | 0 | 0 |
| 1933 | 101 | 0 | 7 |
| 1934 | 79 | 0 | 2 |
| 1935 | 106 | 0 | 1 |
| 1936 | 99 | 1 | 2 |
| 1937 | 116 | 0 | 4 |
| 1938 | 125 | 0 | 2 |
| 1939 | 78 | 0 | 2 |
| 1940 | 75 | 1 | 1 |
| 1941 | 95 | 1 | 0 |
| 1942 | 98 | 1 | 0 |
| 1943 | 99 | 1 | 0 |
| | 1,089 | 5 | 21 |

with a double mitral lesion and cardiac enlargement. She had severe cardiac failure at the seventh month of pregnancy, recovered and was delivered at the eighth month under local anesthesia by elective classical cesarean section with tubal ligation. There was no excessive blood loss and recovery was uneventful.

Let us now turn to the 1,038 patients with rheumatic heart disease delivered vaginally with no fatalities. One hundred thirty-six were in

TABLE X. VAGINAL DELIVERY IN CLASS 3 OR CLASS 4 RHEUMATIC HEART DISEASE

| | ABORTION—35 | | VIABLE BABY—101 | |
|-------------------------------------|-------------|---------|-----------------|-----------|
| | CLASS 3 | CLASS 4 | CLASS 3 | CLASS 4 |
| Number of cases | 35 | 0 | 67 | 34 |
| Deaths | 0 | 0 | 0 | 0 |
| Auricular fibrillation | 3 | 0 | 1 | 3 |
| Cardiac enlargement MI. MS. | 35 | 0 | 67 | 34 |
| Cardiac enlargement MI. MS. AI. AS. | 2 | 0 | 6 | 1 |
| Cardiac enlargement MI. MS. AI. | 2 | 0 | 4 | 6 |
| Primipara | | | | |
| spontaneous | 2 | 0 | 9 | 3 |
| operative | 7 | 0 | 21 | 10 |
| average duration labor | | | | 17 hours |
| Multipara | | | | |
| spontaneous | 3 | 0 | 24 | 14 |
| operative | 23 | 0 | 13 | 7 |
| average duration labor | | | | 10 hours |
| Average weight of babies | | | | 3,440 Gm. |
| Normal pelvis | 30 | 0 | 60 | 33 |
| Age 35 or over | 1 | 0 | 25 | 4 |
| Elderly primigravida | 0 | 0 | 3 | 2 |
| Adequate digitalis | 3 | 0 | 30 | 34 |
| General anesthesia | 32 | 0 | 58 | 22 |
| Local anesthesia | 3 | 0 | 4 | 8 |
| No anesthesia | 0 | 0 | 5 | 4 |
| Post-partum hemorrhage | 0 | 0 | 6 | 1 |
| Average measured blood loss | | | | 170 c.c. |
| Tubal sterilization | 0 | 0 | 4 | 1 |
| Prolonged labor 30 hours or over | | | 8 | 2 |
| Cardiac failure before pregnancy | 0 | 0 | 0 | 7 |
| Cardiac failure ante partum | | | | 21 |
| and intrapartum | | | | 8 |
| and post partum | | | | 1 |
| Month of ante-partum failure | | | Month | 123456789 |
| | | | Cases | 2414 10 |
| Cardiac failure intrapartum | | | | 5 |
| Cardiac failure post partum | | | | 1 |

TABLE XI. SUMMARY OF ABDOMINAL AND VAGINAL DELIVERY IN CLASS 3 AND CLASS 4 RHEUMATIC HEART DISEASE

| | ABDOMINAL | VAGINAL |
|-------------------------------------|-----------|---------|
| Number of cases | 26 | 136 |
| Cardiac enlargement MI. MS. | 26 | 136 |
| Cardiac enlargement MI. MS. AI | 3 | 12 |
| Cardiac enlargement MI. MS. AI. AS. | 2 | 9 |
| Auricular fibrillation | 3 | 7 |
| Primipara | 11 | 52 |
| Multipara | 15 | 84 |
| Age 35 or over | 9 | 30 |
| Elderly primigravida | 2 | 5 |
| Adequate digitalis | 24 | 67 |
| General anesthesia | 18 | 112 |
| Local anesthesia | 8 | 15 |
| Postpartum hemorrhage | 0 | 7 |
| Severe cardiac failure (Class 4) | 15 | 34 |
| Deaths | 3 | 0 |

Class 3 or Class 4. Thirty-five had abortions and one hundred one had viable deliveries. The cases are completely analyzed in Table X. Table XI summarizes the significant data in the abdominal and vaginal groups.

Discussion

One is impressed by the low mortality in this large series. The results are primarily due to good ante-partum care. All patients with organic or suspected heart disease are referred to a special cardiac clinic where those with organic heart disease are classified according to the New York Heart Association criteria. Exercise tolerance and vital capacity tests not infrequently belie a favorable history. We have found the functional capacity very valuable in management and prognosis. Hamilton and Thomson⁴ prefer to classify patients as "favorable" or "unfavorable" and find that 18 per cent originally classified as "favorable" change to "unfavorable" during the course of pregnancy. They conclude that "any cardiac may fail at any time" and recommend following all cardiac patients at weekly intervals throughout pregnancy. We have found no such instability of patients classified according to the New York Heart Association criteria, and we believe the vast majority of Class 1 and Class 2 will go through pregnancy and labor without cardiac difficulty. Accordingly, these cases may be seen in the special cardiac clinic at three- to four-week intervals during the first two trimesters. Any patient more serious than Class 2, or with a history of previous decompensation is admitted to the hospital for study, and early pregnancy may be interrupted if indicated. If the pregnancy is allowed to continue, the patient is either discharged to be carefully followed in the cardiac clinic and later readmitted as indicated, or in some instances, she is kept in the hospital under constant supervision. It is important to note that two of the five ante-partum cardiac deaths occurred after discharge from the hospital following recovery from failure. Such cases should remain under observation in the hospital for the duration of pregnancy. The data indicate the danger of failure begins about the fifth month. Eight (15 per cent) of the fifty-four Class 4 patients died.

The notion that severe cardiacs have a higher than normal incidence of spontaneous abortion or premature labor has led some to expect the patient to solve her own problem. In a previous study Stander⁷ has shown that "cardiac disease in the mother does not increase the loss in offspring by increasing either the ratio of spontaneous abortions or the infantile mortality. The term "infantile mortality" includes all stillborn and deadborn babies weighing more than 1,500 grams as well as those babies dying during the first two weeks of life. The only way in which cardiac disease may affect the infant loss is indirectly through the number of therapeutic abortions performed because of the cardiac disease." In the present series of the one hundred thirteen Class 3, and fifty-four Class 4 patients, the incidence of therapeutic abortion was 18 per cent, and that of spontaneous abortion was 4 per cent. The incidence

of therapeutic and spontaneous abortion in the total clinic population is 0.8 per cent and 5 per cent, respectively. Furthermore, it is noteworthy that there were no spontaneous abortions in the Class 4 patients, or those with auricular fibrillation. The average weight for the viable babies delivered vaginally of Class 3 and Class 4 patients was 3,440 grams, whereas that for the total clinic population is 3,428 grams.

In the cardiac clinic, emphasis is laid upon sodium and fluid restriction, adequate rest, treatment of anemia and upper respiratory infection. Oppel* has shown the importance of anemia and upper respiratory infection as precipitating causes of failure. Any Class 3 patient with a serious upper respiratory infection is admitted to the hospital for observation and treatment. Class 3 patients are generally admitted to the hospital several weeks prior to the expected date of confinement for evaluation and digitalization as indicated. Exercise tolerance tests may precipitate cardiac failure and they are not performed indiscriminately.

The present study of one hundred sixty-two Class 3 and Class 4 cardiacs who were delivered shows a mortality of 12 per cent following abdominal delivery as compared to zero following vaginal delivery. All the abdominal operations were of the elective classical type without hemorrhage. There were five hysterotomies with one death (20 per cent), and twenty-one cesarean sections with two deaths (9.5 per cent).

There was nothing in the histories of the abdominal group which would necessarily make them appear as the most serious cases. There can be no doubt of the severity of the vaginal group which included thirty-four Class 4 cases, and seven with auricular fibrillation. The data also indicate that abdominal delivery has been performed with decreasing frequency in Class 3 and Class 4 patients. Yet, there is certainly no justification for the statement that hysterotomy or cesarean section should never be performed for rheumatic heart disease. There are patients with advanced mitral stenosis who grow progressively worse and die undelivered in spite of all therapeutic measures. The five ante-partum cardiac deaths in this series still present a challenge in the problem of management and perhaps abdominal delivery might have averted the fatal outcome. It should be emphasized that each patient has to be individualized regarding treatment. Complications such as cephalopelvic disproportion, dystocia labor, placenta previa, etc., resolve themselves primarily into obstetric problems and should be so treated. But barring such obstetric indications for cesarean section, the vast majority of cardiac patients are allowed to go into labor spontaneously. It seems that premature interference adds to the existent circulatory burden which is generally greatest between the fifth and eighth months of pregnancy.

The present study does show quite clearly that Class 3 and Class 4 patients can be successfully delivered by the vaginal route. When indicated, vaginal therapeutic abortion is a relatively safe procedure for interruption of early pregnancy. Hysterotomy apparently carries a

definite risk. The hazards of labor can be definitely reduced with good ante-partum care, careful functional evaluation, adequate digitalization, and shortening of the second stage. The pulse and respiratory rates intrapartum provide a valuable guide to the cardiac status. Any patient with cardiac enlargement and a pulse rate above 110 per minute and respiratory rate above 24 per minute, or with such elevation of the pulse rate alone during the first stage of labor should be rapidly and completely digitalized. She should be kept upright in bed, given oxygen, and delivered as soon as feasible after full cervical dilatation to avoid the bearing-down efforts of the second stage. The upright position should be maintained during delivery. Analgesia during labor is used as indicated, but excitement and restlessness are avoided. The choice of drugs depends largely upon the progress of labor.

The data do not support the belief that severe cardiacs have relatively short labors. The average duration of labor in the Class 3 and Class 4 cases was seventeen hours for primigravida and ten hours for multigravida. These values are not significantly different from those in normal women (eighteen hours and twelve hours, respectively) considering that about 50 per cent of the Class 3 and Class 4 cardiacs were delivered by forceps at the end of the first stage of labor. Furthermore, the incidence of prolonged labor in the Class 3 and Class 4 cardiacs was 10 per cent, whereas that for the total clinic population is 9 per cent.

The present study does not corroborate the statement that cardiac patients have a greater than normal blood loss at parturition. The average measured blood loss at delivery in the Class 3 and Class 4 patients was 170 c.c., whereas that for the total clinic population is 247 c.c. We have been favorably impressed with the use of pudendal block for delivery. There is less bleeding with local anesthesia than with open drop ether. Despite the early favorable comment regarding caudal anesthesia, we have not chosen to add the risk of this method to that already existent in the patient.

The avoidance of puerperal infection is always stressed since the damaged heart valve is a locus minoris resistentiae for development of subacute bacterial endocarditis. A program of prophylactic sulfonamide therapy during labor and the puerperium is under way with this end in view.

Such a regimen as outlined above requires all the skill and niceties of medical and surgical obstetrics, and only when these are available should one feel justified in assuming the responsibility for pregnancy complicated by serious rheumatic heart disease.

Summary

A series of 1,089 patients with pregnancy complicated by rheumatic heart disease is presented. This complication occurred in 2.6 per cent of 41,459 pregnancies. The functional capacity diagnoses according to the New York Heart Association criteria were: 480 (44 per cent) Class

1, 442 (41 per cent) Class 2, 113 (10 per cent) Class 3, and 54 (5 per cent) Class 4.

The total mortality was 11 (1 per cent), and the cardiac mortality 8 (0.7 per cent). All cardiac deaths were due to decompensation—five died undelivered, and three died following abdominal delivery.

The Class 3 and Class 4 cases are completely analyzed. Twenty-six were delivered abdominally with 3 deaths (12 per cent). One hundred thirty-six were delivered vaginally with no deaths. The abdominal group consisted of 5 hysterotomies with 1 death, and 21 cesarean sections with 2 deaths. The vaginal group consisted of 35 abortions and 101 viable deliveries.

Cardiac failure occurred after the fourth month, and 15 per cent of these cases died.

An outline for management of pregnancy complicated by serious rheumatic heart disease (Class 3 and Class 4) is presented.

Conclusions

1. The successful management of pregnancy complicated by serious rheumatic heart disease requires a program of medical and surgical obstetrics of the highest order.

2. Barring other obstetric complications, the vast majority of cases can be successfully delivered by the vaginal route.

3. When indicated, vaginal therapeutic abortion is a relatively safe procedure for interruption of early pregnancy.

4. The hazards of labor can be definitely reduced with good antepartum care, careful functional evaluation, adequate digitalization and shortening of the second stage. The pulse and respiratory rates intrapartum provide a valuable guide to the cardiac status.

5. Abdominal delivery has been performed with decreasing frequency, yet it may still have its place in those patients who fail to improve in spite of treatment.

6. Each patient should be evaluated as an individual problem.

7. Once severe cardiac failure has occurred antepartum, there is a great risk in discharging the patient from the hospital before delivery.

8. The incidence of spontaneous abortion and premature labor, the duration of labor and the blood loss at parturition in women with serious rheumatic heart disease are not significantly different from values in normal women.

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BACTERIOLOGIC AND CLINICAL ASPECTS OF GONORRHEA IN THE FEMALE*

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Section I: Bacteriologic Aspects

A STUDY of gonorrhea in the adult female was initiated by the Gonococcus Research Unit of the Department of Health, City of New York, in October, 1942. This study was deemed necessary because of the belief that the control of gonorrhea in general, depends to a great extent, upon effective control of gonorrhea in the female. The aims of the study were, therefore, to evaluate and improve the methods of diagnosis and the criteria of cure in current use, and to determine the effectiveness of various methods of therapy.

Two agencies participated in this study; (a) The gynecological service of Bellevue Hospital; and (b) the clinic and laboratory of the Gonococcus Research Unit, Department of Health, City of New York.

The present report which covers a period of nine months, is concerned mainly with observations on hospitalized patients, many of whom were subsequently followed up at the clinic of the Research Unit. Patients for this study were selected by the members of the staff of the gynecological service, on the basis of a suggestive history, or suspicious clinical symptomatology, or both. A few cases with a diagnosis of gonorrhea were referred by the clinic of the Department of Health.

For the purpose of simplifying the analysis of the numerous problems involved in this study, it was decided to divide this report into two separate sections. The first part deals with the bacteriologic aspects of female gonorrhea, while the second part evaluates clinical features.

During the course of the routine bacteriologic examinations of 230 female patients, the following problems came under consideration: the relative merits of smears and cultures in the diagnosis of gonococcal infections in the female; the limitations of smears and cultures and a re-evaluation of bacteriologic examination of operative gynecological specimens.

Bacteriologic Diagnosis

Collection of Material.—All patients were examined bacteriologically by smear and culture taken according to the procedure recommended by

*This investigation was aided by a grant from the United States Public Health Service.

the American Neisserian Medical Society. Smears and cultures were taken from both the urethra and cervix at each examination.

Smears.—Smears were usually examined first so that the smear diagnosis would be uninfluenced by the culture results. A smear was considered gonococcus positive if intracellular gram-negative diplococci of typical appearance and arrangement were present. It was recorded as suspicious if similar organisms were found extracellularly.

Cultures.—Swabs inoculated with the exudate were transported to the laboratory in tubes containing 2 per cent Difco Proteose Peptone No. 3 Water. The culture material was inoculated onto solid media within a period of 3 to 5 hours after being collected. Throughout the study, two plates containing different media were used for each culture. One was a standard medium proved to be satisfactory for the growth of the gonococcus. This consisted of Difco Proteose No. 3 Agar as a base with an enrichment of 5 per cent hemolyzed horse blood and 8 per cent ascitic fluid. The second plate contained a medium with the same base, Difco Proteose No. 3 Agar to which had been added any one of a number of biologicals and chemicals in an attempt to study their effect on the culture growth of the gonococcus. The effects of vitamin B₁₂, para-amino benzoic acid, liver extract, lysine, hemolyzed human and beef blood, dextrose, cysteine monohydrochloride and tyrothricin were studied. The only positive effect observed was an increase in the size of the colonies when vitamin B₁₂, liver extract or cysteine monohydrochloride were added to the medium.

The cultures were incubated in an atmosphere of 12 per cent CO₂ tension at 35° C. for 24 hours, and then without CO₂ for another 24 hours before being examined by two experienced technicians. The oxidase test was used only to ascertain that no suspicious colony had been overlooked. Suspicious colonies were examined microscopically and fished for subcultures. A strain was identified as a gonococcus, if it fermented only dextrose, showed no hemolysis on 5 per cent horse blood agar and none or only weak growth on plain agar.

Laboratory Findings.—Three hundred and seventeen hospitalized patients were examined by smears and cultures during the observation period from October 13, 1942, to June 30, 1943, and a total of 1,759 bacteriologic examinations were performed upon them. Of the total number of patients, 87 had to be excluded from the following analysis because of incomplete observation due to lack of cooperation on the part of the patient, or for other reasons. Of the remaining 230 women, 91 (39.5 per cent) were diagnosed as gonococcus positive by either cultures or smears or both.

On the basis of the results obtained from the initial culture or smear examinations, 8 of the 91 infected patients were found to have an infection limited to the urethra and 46 others, an infection of the cervix alone. In 37 cases both urethra and cervix were found to be infected. The concurrent involvement of urethra and cervix nearly equaled that of the cervix alone.

Comment

As may be seen in Table I cultures were found to be far more accurate than smears. More than half of all gonococcus positive cases would have been lost, if the diagnosis had been based on smears alone.

On the other hand, eight negative cultures were accompanied by two suspicious urethral and six suspicious cervical smears. Whether the

TABLE I. RESULTS OF URETHRAL AND CERVICAL SMEARS AND CULTURES IN A GROUP OF 91 GONOCOCCUS POSITIVE CASES

| URETHRA | | | CERVIX | | |
|----------------------|-------------------|-------------------|-----------------------|-------------------|-------------------|
| SMEARS | CULTURES | | SMEARS | CULTURES | |
| | CULTURES POSITIVE | CULTURES NEGATIVE | | CULTURES POSITIVE | CULTURES NEGATIVE |
| Smears positive: 8 | 6 | 2* | Smears positive: 21 | 20 | 1† |
| Smears suspicious: 7 | 5 | 2 | Smears suspicious: 14 | 8 | 6 |
| Smears negative: 30 | 30 | — | Smears negative: 48 | 48 | — |
| Total: | 41 | 4 | Total: | 76 | 7 |

*Cultures overgrown.

†Culture sterile.

cultures actually failed in these cases is open to question, since the organisms diagnosed as suspicious on the smears may have been any of the gram-negative organisms resembling the gonococcus which are commonly found in the female genital tract. Furthermore, it is possible that the organisms observed in the smears were gonococci which were no longer viable. Since treatment was initiated in these eight cases immediately after the first examination, no further bacteriologic identification was possible.

Limitations of the Bacteriologic Diagnosis.—Although a diagnosis of gonorrhea may be presumed from a suggestive history and from both clinical and epidemiological findings, the etiologic agent of the infection can only be determined by bacteriologic methods. These methods, however, like any other biologic tests are subject to certain definite limitations,^{1, 2} the causes of which are still debated and not completely understood.

In previous studies,³ it has been observed that results of smears taken from untreated patients in the advanced acute stages of the disease fluctuated from positive to negative and were therefore unreliable. This observation also holds true for the cultures, although the fluctuations appear much later, at a much more advanced stage of the infection.

Little is known of the actual factors interfering with the accuracy of the bacteriologic methods, although several explanations have been advanced. One view stressed by the Gonococcus Research Unit emphasizes the fact that biologic changes in the infected tissues and the resulting action on the organisms may cause anatomic or immunologic reactions which decrease the viability and number of the gonococci. These changes may gradually lead to a temporary or permanent hidden focus of gonococci within the deeper layers of the invaded tissues or may occasionally cause their complete destruction. These conditions are designated clinically as chronic gonorrhea, latent gonorrhea and spontaneous cure respectively.

Other investigators² believe that the limitation of the culture diagnosis is due chiefly to a lack of sensitivity of our present culture media. Experimental evidence indicates that a minimal number of viable

organisms must be present before a positive culture can be obtained. With the available culture media, this minimum represents a very large number of organisms. The ideal medium would be one sensitive enough to promote growth when only a single viable organism is present in the pus specimen.

The problem of the limitations of gonococcus culture diagnosis is therefore a complex one. There is ample clinical and experimental evidence to indicate that both factors probably play some part in limiting the accuracy of the bacteriologic findings. From the clinical point of view this limitation appears to be caused by a temporary or prolonged latency of the infection. The solution of the bacteriologic problem depends upon the development of culture methods which will insure growth of small numbers of organisms. Prolonged observation and repeated bacteriologic examinations will minimize the shortcomings of our present bacteriologic diagnostic methods.⁴

Operative Material.—Operative gynecologic material for bacteriologic examination was obtained from 19 patients. Of these 19 cases, 11 had a negative history and negative bacteriology and received no chemotherapy prior to their operation. Another patient, likewise bacteriologically negative, had a history of gonococcal infection 18 years previously. She received 12 grams of sulfathiazole because of salpingitis for which she was subsequently operated upon. Seven other cases were diagnosed as gonococcus positive upon admission; 6 were treated with sulfathiazole while the seventh did not receive any treatment prior to operation.

Bacteriologic material for smears and cultures were taken from 14 inflamed Fallopian tubes, 7 ovaries, 2 uterine cavities and from a ruptured tuboovarian abscess. After surgical removal, the different organs were opened and any exudate present on the surface of the mucous membrane was taken up by a sterile swab which was immersed into peptone water. The mucous membrane was then scraped with a sterile knife in order to obtain exudate from the deeper layers of the inflamed tissue. In some cases pieces of tissue were excised, immersed in peptone water and ground up in a mortar before final inoculation onto the culture media.

All of this operative material yielded negative bacteriologic findings. These results seem to contradict the previous observations of Studdiford, Casper and Seadron.⁵ Further studies of untreated infected patients are necessary, since all but one of the gonococcus-positive patients included in our series, received chemotherapy prior to their operation.

Summary and Conclusions

1. This study deals with a bacteriologic analysis of 230 patients from the gynecological service at Bellevue Hospital.

2. Ninety-one women were found to be gonococcus positive either by smear, or culture or both. Eight of these women had a gonococcal infection of the urethra alone, while in 46 cases only the cervix was

involved. Thirty-seven patients suffered from a concurrent infection of the urethra and cervix.

3. Cultures were found to be far more accurate than smears. More than half of all positive cases would have been missed if the diagnosis had been based on smears alone.

4. Limitations of the culture diagnosis in the advanced stages of the infection may be due to either a lack of sensitivity of our present culture media, or to a temporary or persistent latency of the disease.

5. The bacteriologic examination of the operative gynecological material obtained from 19 cases yielded negative results.

6. Seven of these 19 cases were originally gonococcus positive in the urethra or cervix, and 6 of them had received chemotherapy prior to operation.

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Section II. Clinical Aspects

This clinical section presents an analysis and a discussion of therapy in sulfonamide-resistant and responsive patients, and describes several provocatives tested in an attempt to improve the criteria of cure. In addition, the clinical findings in infected patients before and after treatment and in uninfected cases were analyzed and compared. The results of this comparison led us to attempt to determine whether or not the term "clinical gonorrhea" is valid and its use justified.

Clinical Aspects

Clinical Record.—A complete clinical history was taken on each of the 230 patients examined. This history included a record of the duration of complaints, the time of exposure, previous infections and previous treatment. The amount of the urethral and cervical discharge, the presence or absence of secretions from the Skene and Bartholin glands, and the findings of adnexal involvement were all recorded.

Adnexal Involvement.—Of the 91 patients found to be gonococcus positive, 72 (79 per cent) showed an involvement of the adnexa. This high figure does not represent the true frequency of the complication in gonococcal infection in general, but is due to the fact that most of the patients required hospitalization because they were suffering from some pelvic inflammatory disease.

A similar high percentage (82 per cent) of adnexal involvement was found in the 139 patients with a negative history and negative bacteriologic examinations. It is nevertheless possible that a certain percentage of these adnexal involvements may have been residual inflammations due to previous gonococcal infection in spite of the fact that no definite history of previous gonococcal infection was obtainable. Nevertheless, in the 11 untreated cases from which operative material was examined bacteriologically, no gonococcus-positive bacteriologic results were obtained. On the basis of our present diagnostic methods, all of these 139 patients had to be considered free from gonococcal infection.

There were 16 additional patients who were bacteriologically gonococcus negative. However, they were not included in the analysis of this particular group of uninfected cases because they gave a definite history of previous gonococcal infection.

Involvement of Bartholin and Skene Glands.—An inflammation of the Bartholin glands was found in 18 patients, half of whom had a gonococcal infection. Discharge of the Skene glands was observed in 12 gonococcus-positive patients, and in 8 gonococcus-negative women.

Treatment.—Sulfathiazole was used as the drug of choice throughout the study because of the high percentage of cures obtained and the relative absence of toxic side effects.¹

Because of the short period of hospitalization of patients at Bellevue Hospital, arbitrary standards for the determination of cure had to be adopted. It was decided to assume that a patient was "cured" if three consecutive negative cultures and smears were obtained following treatment. If only two negative results were available, the patient was assumed to be a "probable cure." These are the criteria which are used throughout the following discussion.

Of the 91 patients found to be gonococcus positive, 21 are not included in this discussion either because they signed out of the hospital before therapy could be administered or cure determined, or because they received different amounts of various sulfonamides.

Two treatment schedules were followed during the period covered by this report. The first, which followed the routine of therapy already in use in the gynecological service, consisted in the administration of a total of 21 grams of sulfathiazole, in doses of 3 grams each, given over a period of seven days.

Of the 23 patients who received this amount of sulfathiazole, 13 were cures, 6 were probable cures and 4 patients were resistant to treatment.

The average follow-up of cured cases in this group was 20 days (max. 44; min. 8), with an average of 4.6 negative bacteriologic examinations (Max. 7; min. 3). The probable cures were examined twice over an average period of 7.4 days (Max. 10; min. 2). Four of the patients in this whole group attended the research clinic for an additional follow-up period of 26.7 days (max. 51; min. 11) and an average of 4.2 examinations were performed (max. 6; min. 3). All of these patients remained bacteriologically negative during follow-up observations.

In the second treatment schedule, the daily dosage of sulfathiazole was increased to 4 grams and given over a period of 3 days so that the total dosage administered was only 12 grams.

The remaining forty-seven patients in the infected group were treated according to this schedule of therapy. Of this total, 35 were cures, 5 were probable cures and 7 were found to be resistant to treatment.

The cured patients in this group were followed up for an average of 13.8 days (Max. 39; min. 7) and 4.7 bacteriologic examinations (max.

10; min. 3) were performed. The 5 probable cures were examined and found negative twice over a period of 4.4 days (max. 9; min. 2). Sixteen of the women in this group reported to the research clinic for an additional follow-up. An average of 3.5 examinations was performed on them (max. 9; min. 1) over a period averaging 29.5 days (max. 133; min. 6). All of these patients remained negative during the follow-up period.

It appears from these observations that slightly larger daily doses over a short period of time yielded results which are just as good, if not better, than those obtained with smaller daily doses over a longer period.

Sulfonamide-Resistant Gonorrhea.—Although no exact figures are available, the prevailing impression is that the number of sulfonamide-resistant gonococcal infections is increasing. There are many factors which may be responsible for failure of chemotherapy; among them the inadequate and irregular administration of chemotherapeutic compounds which especially in cases of self-medication, may frequently lead to a gradual drug-fastness of the organisms. This drug-fast strain may be subsequently transmitted to a new host. Another factor involved in resistance to sulfonamides, was brought out by recent studies which show that primarily sulfonamide-resistant gonococcus strains can be isolated from patients prior to chemotherapy.² The in vitro behavior of these strains corresponds in most cases to the clinical reaction of the patient. However, some patients respond readily to sulfonamide therapy despite the fact that they do harbor an in vitro-resistant strain. This indicates that a host factor exists, separate and distinct from the strain factor and that it plays an important, if not the decisive role in the response to therapy. The exact nature of this human host factor is not yet known, but it is most likely related either to the natural resistance of the human host to any infection in general, or to a specific immunologic response.

Among the 91 gonococcus-positive women 14 (15.3 per cent) were found to be resistant to sulfonamide therapy. All strains isolated from these patients likewise proved to be resistant in vitro. Four patients were initially treated with 21 grams, and 7 with 12 grams of sulfathiazole, while the remaining 3 patients received varying amounts of different sulfonamides. Of these 14 cases, 6 were lost for further study.

Various methods of treatment were tested in an attempt to develop a simple and effective therapy for these resistant cases. A combination of gonococcus vaccine and sulfathiazole was used in five of the eight resistant cases, which had been found to be of value in the treatment of sulfonamide-resistant gonorrhea in the male.³ The vaccine was injected subcutaneously, ten injections being given on alternate days. The sulfathiazole was administered either orally or locally, following the fifth injection of vaccine. Two of the three patients who received sulfathiazole by mouth were cured, while the third failed to respond to this combined therapy and was subsequently cured by penicillin. Two other patients in the series were cured by local cervical applications of 10 per cent sodium sulfathiazole in one case, and of 20 per cent sodium sulfathiazole with 2 per cent urea in the other case. Both sulfonamide compounds were dispersed in a special wetting agent for more adequate penetration of the drug.* In the first patient, vaginal tampons impregnated with the sulfonamide dispersion were inserted and renewed daily for 7 days. In the second case the following technique was used at the suggestion of Dr. Borris A. Kornblith. A vagi-

*This product was made available to us through the courtesy of the Wallace Laboratories, Inc., New Brunswick, N. J.

nal diaphragm was introduced into the vagina in such a manner, that the posterior portion of the rim was fixed in the posterior fornix so that the rubber cup covered the cervix. The anterior rim was then prised away from the anterior vaginal wall just enough to permit the injection of 5 c.c. of the fluid medication into the diaphragm cup by means of a Luer syringe to which a 2½ inch extension was attached. The anterior rim of the diaphragm was then pushed back underneath the symphysis pubis. No medication was lost by this method and an intimate contact of cervix and sulfathiazole dispersion was assured. The diaphragm was changed every day for 7 consecutive days.

The 3 remaining patients in this series of resistant cases were treated only with repeated courses of oral chemotherapy. One of them responded to a second course of 21 grams of sulfathiazole; the second patient remained resistant to repeated administration of various sulfonamides and finally became cured spontaneously; while the third failed to respond to 3 courses of sulfathiazole (12, 28, 28 grams) administered while she was under our observations.

We shall make no attempt to comment on these cases since the number is entirely too small to permit any conclusions to be drawn. The description of the various techniques used has been introduced to indicate different methods of approach to the problem of cure of sulfonamide-resistant gonorrhea in females.

Provocatives.—In order to place the determination of cure in the female on a more reliable basis, an effective provocative agent must be found. Various biological and chemical methods such as specific or nonspecific vaccines, the local application of iontophoresis, of Lugol's solution, and of various concentrations of zinc sulfate, silver nitrate, glycerin and hydrogen peroxide had been tested previously without any success. The value of menstruation as a physiologic provocative was studied and it was found out that cultures taken before, during or after the menstrual period would occasionally yield positive results. These results can form no basis for judging the value of menstruation as a provocative, since similar occasional positive bacteriologic findings were also obtained on routine examinations.

The ideal provocative is one which will produce an irritation of the cervix without affecting either the adnexa or the gonococcus itself. The first of several provocatives tested during the study was sterile dermal suture material which was inserted into the distal third of the cervical canal and kept there for a period of 24 hours. In 4 patients who were being followed up for determination of cure, the presence of the dermal suture did not produce any cervical irritation or adnexal flare-up. No positive cultures were obtained following the use of this method.

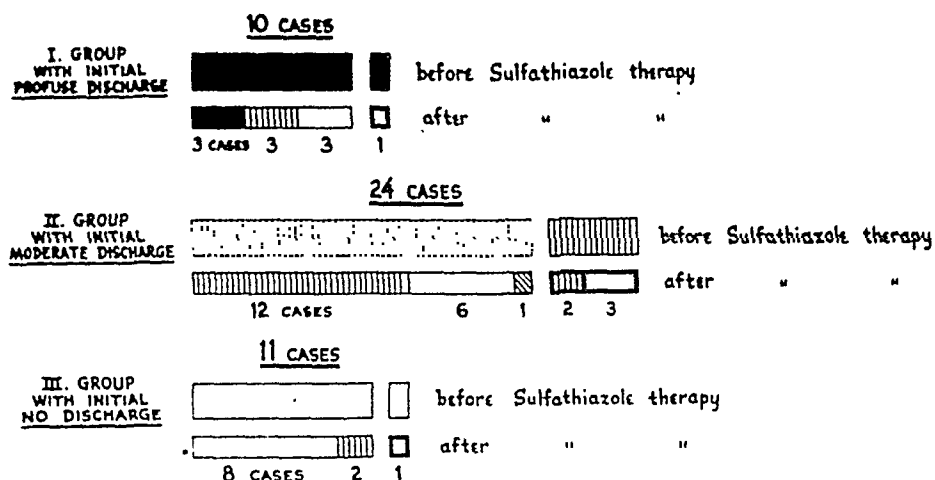
Cauterization of the vaginal portion of the cervix was the second provocative tested. This method had previously given promising results when tested in the Welfare Island Dispensary (Dr. Pellegrino). At Bellevue Hospital, 37 patients who had been initially gonococcus positive and had become bacteriologically negative after chemotherapy, were cauterized and all of them remained negative. Cauterization which was generally painless, was followed in all cases by a definite increase in the amount of the cervical discharge, lasting from 2 to 4 days. No adnexal flare-up occurred even in those cases where previous inflammation of the adnexa had existed.

The provocative effect of 6 grams of sodium chloride kept in close contact with the cervix for 24 hours by means of a vaginal diaphragm

was the last method tested. The diaphragm was inserted in the manner previously described for the local use of sulfonamide dispersions. If the salt was left in contact with the cervix for more than 3 days, a superficial maceration of the cervix and of the anterior vaginal walls

GONORRHEAL URETHRITIS - 45 CASES

A COMPARISON OF THE AMOUNT OF URETHRAL DISCHARGE BASED ON EXAMINATION BEFORE AND AFTER SULFATHIAZOLE THERAPY



GONORRHEAL CERVICITIS - 83 CASES.

A COMPARISON OF THE AMOUNT OF CERVICAL DISCHARGE BASED ON EXAMINATION BEFORE AND AFTER SULFATHIAZOLE THERAPY

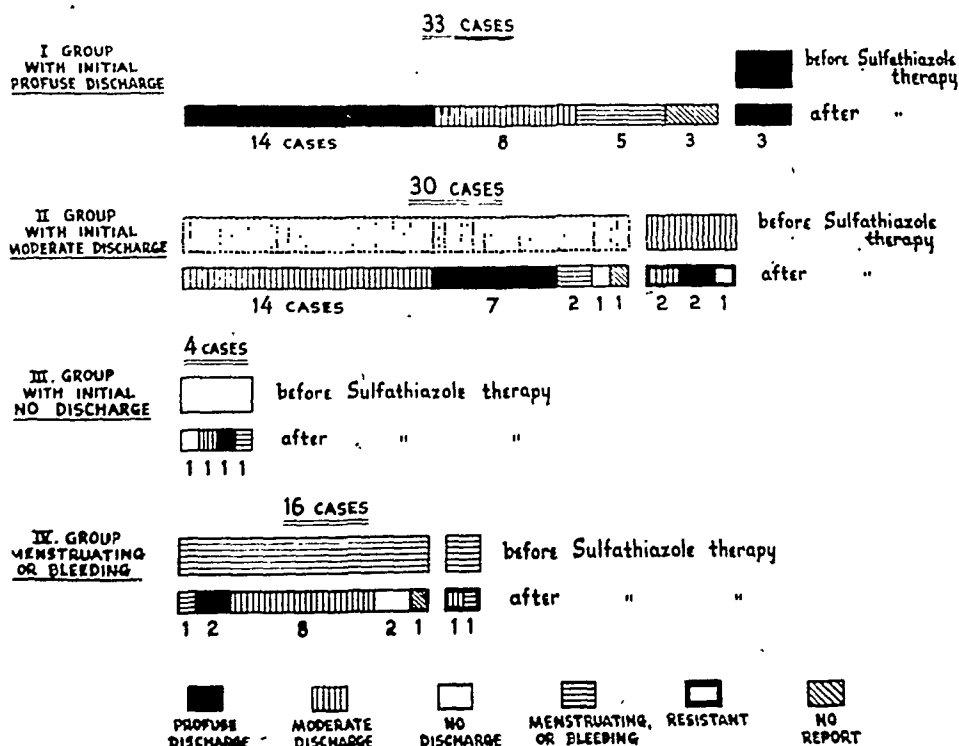


Fig. 1.—Gonorrheal urethritis. Comparison of the amount of urethral discharge based on examination before and after sulfathiazole therapy.

was observed. Considerable increase in the cervical secretion was produced by the salt. In a few gonococcus-positive cases, sterile cultures were obtained following the use of this method, although the bacteriology reversed to positive after a few days. Although the number of cases tested is very small, it appears doubtful that this procedure is likely to prove of practical value as a provocative.

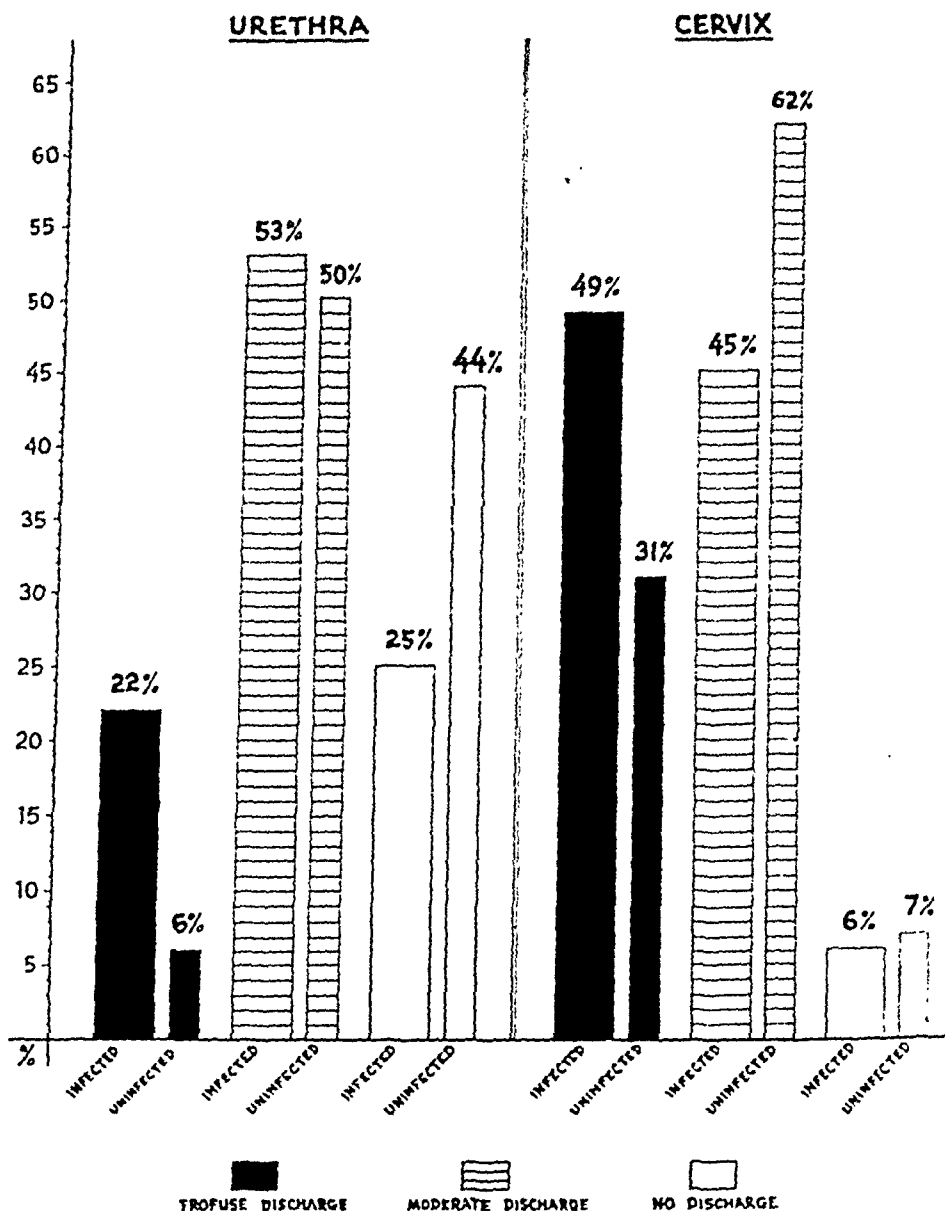


Fig. 2.—Comparison of the amounts of urethral and cervical discharges, on initial examinations, present in 91 infected and 139 uninfected patients.

Evaluation of the Diagnosis of "Clinical Gonorrhea."—Because of the rise in the incidence of venereal diseases, resulting from present war conditions, the recommendation has been made^{1, 4-5} that contact cases with clinical signs suggestive of gonorrhea be treated immediately, even if bacteriologic findings are negative or entirely lacking. Such a recommendation is of practical value in helping to check the spread of infection by sexually promiscuous women who are known sources of infection.

Unfortunately, this recommendation may lead physicians to dispense with the confirmatory bacteriologic results of smears and cultures and to substitute for these a diagnosis of "clinical gonorrhea" based on clinical symptomatology alone.

Such a diagnosis may perhaps be made safely, only in cases of early acute gonococcal infection presenting classical symptoms in which positive bacteriologic findings can be readily obtained. Unfortunately, this typical clinical picture appears less and less frequently,⁶ so that verification of the clinical diagnosis by laboratory methods has become indispensable.

URETHRA - 45 CASES

CERVIX - 82 CASES

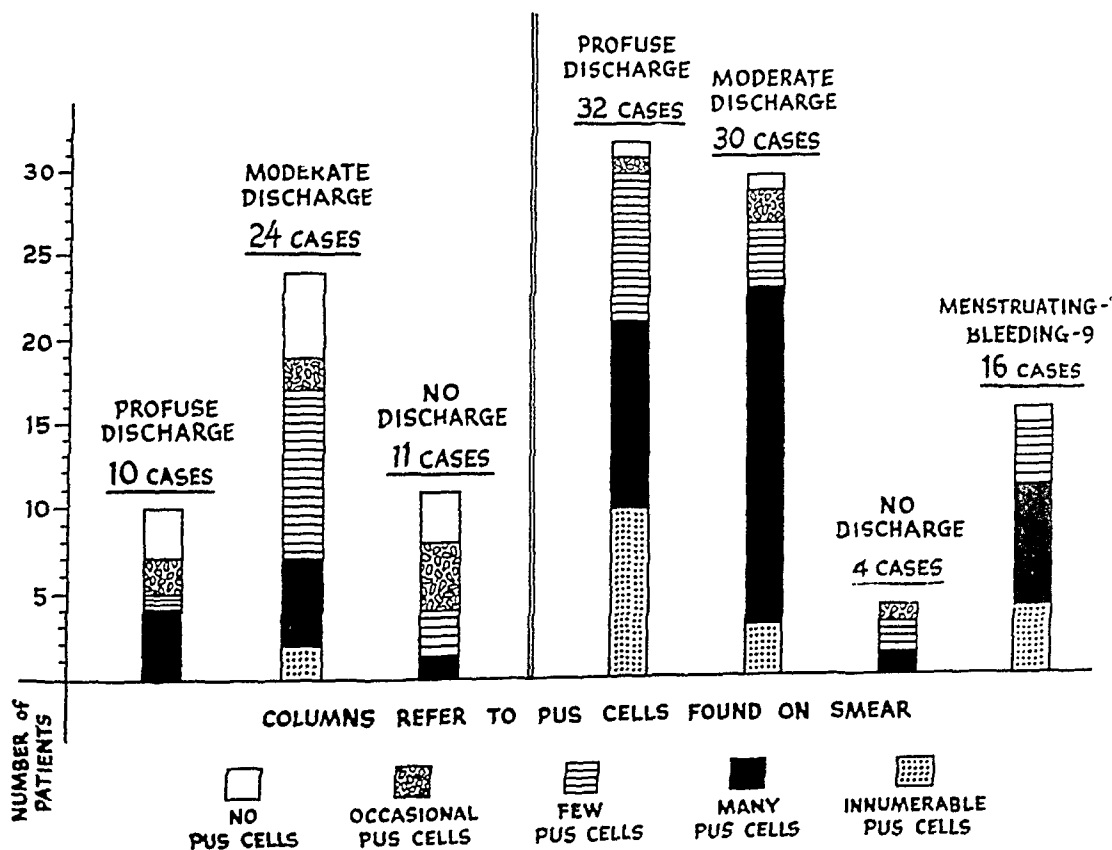


Fig. 3.—Comparison of amount of discharge with number of pus cells in corresponding smears on initial examination in a group of infected patients before treatment.

If a diagnosis of gonococcal infection could be made on the basis of clinical findings alone, there should be appreciable differences between the amounts of discharge present in infected, treated and uninfected patients.

In order to evaluate this concept of "clinical gonorrhea," observations on the discharge present in the urethra and cervix of 230 patients were analyzed.

Comment on Fig. 1.—As can be seen from the illustration, urethral discharge generally becomes less while the amount of cervical discharge either remains the same, or becomes more profuse after successful therapy.

*All initial observations following treatment were made within one to three days after termination of therapy.

Findings Over a Prolonged Period of Observation.—In order to determine whether or not these initial findings after chemotherapy hold true over a longer period of time, observations on the amount of urethral and cervical discharge in treated cases during a period of 2 to 4 weeks were graphically plotted. The following distinct patterns became apparent from these graphs.

Urethral Findings.—Those cases which had no initial urethral discharge remained negative throughout repeated examinations after cure. If the original discharge was moderate, frequent fluctuations from moderate to negative were observed during follow-up, until the majority of patients finally lost all their discharge. Half of the patients with an originally profuse urethral discharge, became completely negative while the other half retained a moderate discharge.

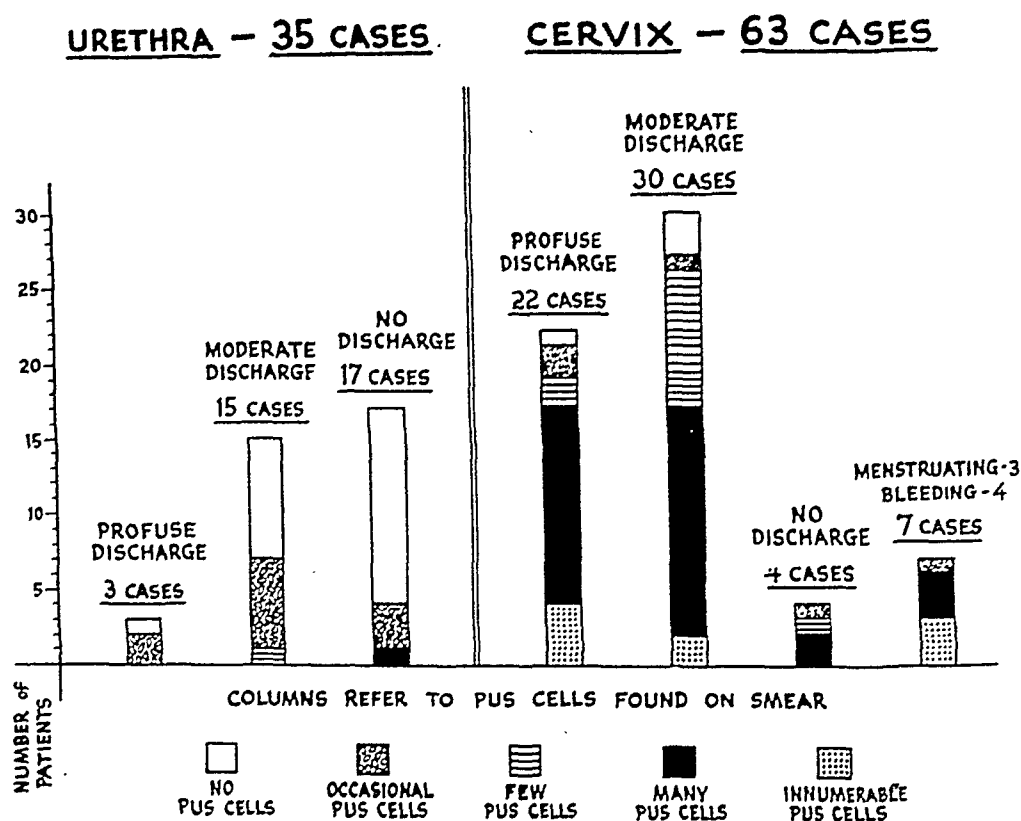


Fig. 4.—Comparison of amount of discharge with number of pus cells in corresponding smears on initial examination in a group of infected patients after treatment.

Cervical Findings.—Patients without any cervical discharge before treatment showed fluctuations in the amount of discharge following therapy. However, the number of these patients (4) is too small for any conclusions to be drawn. Wide fluctuations from moderate to profuse were observed in these patients with an initial moderate discharge. At the end of the 4 weeks' observation period most of the patients still retained their original moderate discharge while a third had developed a profuse discharge. Among the group of women with an initial profuse cervical discharge, there was a limited fluctuation from profuse to moderate during the follow-up period. Half of the patients finally retained their profuse cervical discharge, while the discharge became moderate in the other half.

These observations confirm the results shown in Fig. 1. Cases having urethral discharge before treatment either lose it entirely, or show

a reduction in the original amount of discharge after cure. In the cervix, however, there is no correlation between the amounts of discharge before and after cure. Very few of the patients lost their cervical discharge completely; the majority retained their original amount. In other words, the presence or absence of discharge in the urethra after treatment may be of some assistance in establishing cure. It is of little significance, however, in the case of the cervix since most cases retained their discharge after treatment.

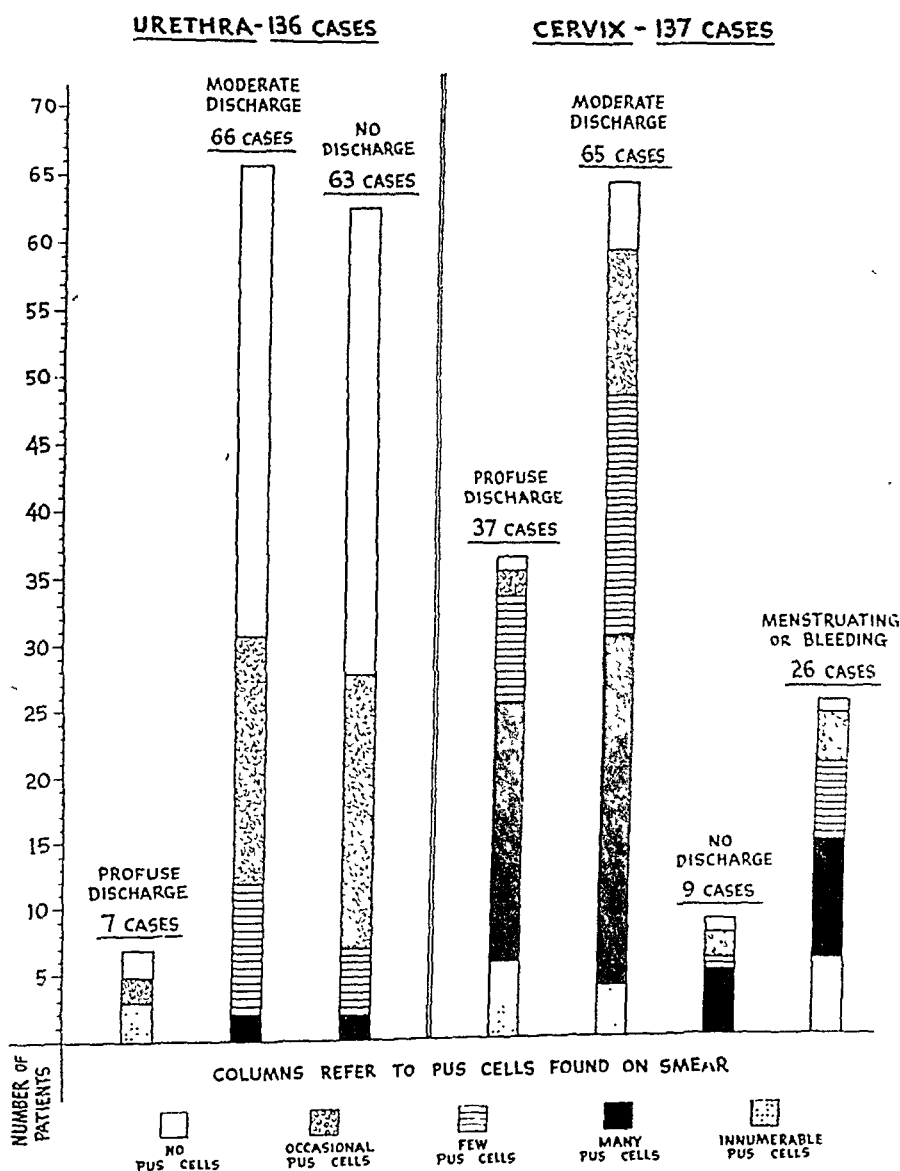


Fig. 5.—Comparison of amount of discharge with number of pus cells in corresponding smears on initial examination in a group of uninfected patients.

Comparison of the Amounts of Urethral and Cervical Discharges of Infected and Uninfected Patients.—The observations on a group of 139 women with negative history and negative bacteriology (average 1.6 examinations)* were compared with the findings on the 91 gonococcus-positive cases. This is shown in Fig. 2.

*Of these uninfected negative cases, 56 were examined bacteriologically at least twice. The results in this group were found to be identical with those obtained in the larger group.

As can be seen from the illustration, the presence of cervical discharge is of little aid in establishing a diagnosis, since over 90 per cent of the patients in both the infected and uninfected groups showed a moderate or profuse cervical discharge. The same holds true to a lesser extent, in the observation on the urethral discharge, where 50 per cent of the patients in both groups showed a moderate urethral discharge.

Comparison of Urethral and Cervical Discharges With the Number of Pus Cells Found on Corresponding Smears.—Color and consistency cannot be regarded as satisfactory criteria for determining the nature of discharge since the interpretation of these characteristics necessarily varies with the observer. The number of pus cells present in the corresponding smears was felt to be a more critical standard, and these findings were therefore correlated with the amount of discharge observed.

Urethra.—As can be seen from Figs. 3 to 5, the amount of urethral discharge was correlated with the corresponding number of pus cells in infected cases only before treatment, but not in treated or uninfected patients. In all 3 groups, pus cells were frequently found to be present in cases in which no urethral discharge was reported.

Cervix.—A close correlation was found between the amount of cervical discharge and the number of pus cells present in the corresponding smears in all three groups. As in the case of the urethra, occasional pus cells were frequently found in cases reported free of discharge.

Comment.—The cervical discharge observed was to a great extent purulent in character. The majority of cases showed this purulent discharge regardless of their bacteriologic status.

Discussion

All these observations clearly indicate that there is no basis for differentiating between infected, treated and uninfected patients by clinical examination alone. The diagnosis and the determination of cure of gonococcal infection in the female must be verified by laboratory methods. The current practice of public health agencies of recommending isolation and treatment of sexually promiscuous women who are known sources of infection, may be justified as a practical measure in checking the spread of gonorrhea.

Since our findings indicate that the term "clinical gonorrhea" cannot be consistently verified and is misleading, it is advisable to eliminate this designation entirely. The term "possible infectious contact" is suggested to designate those cases in which bacteriologic evidence of infection is lacking, but who require immediate treatment as a public health measure.

Summary and Conclusions

1. Adnexal involvement was found in 79 per cent of the infected group and in 82 per cent of the uninfected group.

2. Two schedules of therapy were employed: In one a total dosage of 12 grams of sulfathiazole was given over a period of 3 days, while in the other a total dosage of 21 grams of sulfathiazole was administered over a period of 7 days. The therapeutic results are nearly identical in both groups.

3. Resistance to sulfonamides in gonococcal infections is determined by at least 2 known factors: the presence of a sulfonamide-resistant

gonococcus strain, and the action of a "human host factor," which appears to play the decisive role.

4. Attempts to develop a simple treatment for sulfonamide-resistant gonorrhea are described.

5. The provocative effects of sterile dermal suture material, of cauterization and of sodium chloride were tested and found to be unsatisfactory.

6. Observations on a group of 139 uninfected women, and 91 infected patients indicate that the amount and character of urethral and cervical discharge is of little or no aid in establishing a diagnosis.

7. The term "clinical gonorrhea" is misleading, and does not represent a true clinical entity.

8. The term "possible infectious contact" is suggested for designating sexually promiscuous women who are known sources of infection.

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THE EFFECT OF TRAVEL ON THE INCIDENCE OF ABORTION*

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DEVELOPMENTS, the results of World War II, have produced conditions which permit a different approach to ascertaining the effect of certain environmental factors on disease. Herein lies one such study whereby the geographical location of a prenatal clinic temporarily afforded an evaluation of the effect of travel on the incidence of abortion, which is defined in the strict sense as referring to the first 16 weeks of pregnancy. It is recognized at the outset that the résumé is not complete, the reason being that the natural factors making the observation possible were altered in such a manner that further work was not feasible. Nevertheless, it is felt the results available are worthy of record.

Nowadays with the mass transfer of military personnel and migration of civilians, the doctor is frequently asked the advisability of an expectant mother taking an extended trip. From the experience of three certified obstetricians and gynecologists (A. W. Diddle, R. W. Jack, and R. L. Pearse), who have interviewed 1,058 consecutive obstetric patients between June 1, 1941 and April 1, 1944 with respect to journeys taken and the advice given previously by the family physician, it is apparent that a majority of practitioners were unwilling to sanction tours particularly during the first and third trimester. In textbooks on obstetrics, where mention is made of the subject, the same idea prevails. Although it is agreed that activity helps to evacuate the uterus after other intrinsic and extrinsic factors have threatened an abortion, it has become the opinion of this group that the average means of modern travel, alone, do not predispose directly to the occurrence of the disease. When an abortion occurs in relation to a journey, the two phenomena are regarded as more or less coincidental. Basis for this contention is supported by a study comparing the incidence of abortion among a group of pregnant women who journeyed and a series who maintained a sedentary existence during the period of gestation. As previously inferred, geographic position of the clinic has permitted a study and confirmation of the impression.

To begin, it is pertinent to describe the location of this community. It is situated on an islet five miles long and one to two miles wide. The highest point above sea level is 23 feet. The climate is semi-tropical. The sun shines 360 days out of the year. The seasonal temperature variations range from 55 to 96 degrees Fahrenheit. Al-

*The opinions or assertions contained herein are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

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though there is less than 40 inches of rainfall annually, the humidity is enervating during the period from May to November. The area is 127 miles from the mainland of the Continental United States. The intervening space was spanned by a rough, asphalt and coral highway up to the time the observations were suspended. The route was built over innumerable keys which were joined together by a series of 62 bridges. The thoroughfare for great distances was corrugated with numerous transverse humps. These had been produced by heavy trucks and atmospheric and geologic changes. They caused an occupant of an automobile or bus to experience a drive simulating a ride in a springless vehicle going at a fairly rapid rate of speed. In order to communicate to and from the nearest railroad, 170 miles away, it was necessary for all women and children to go by bus or car over this course.* Thus for purposes of the study all women had a common denominator with regard to the means of entering or leaving the locality which had a population of approximately 40,000 in January, 1944.

The Naval Hospital and Dispensary, from which these data were collected, served all obstetric dependents of the Navy, Marine Corps, Coast Guard and Army personnel with the section concerned.

Food, including fresh vegetables, fruits, and meats, eggs and milk, was as plentiful here as any place in the states. Like other defense areas, tenements were frequently inadequate and crowded particularly for families of enlisted men.

Observations

Patients were represented from all 48 states, two foreign countries and the District of Columbia. A majority came from 26 states most of which were along the eastern seaboard. Included were California and Texas. The distribution gave a fair sampling of women from the entire United States. All the expectant mothers were white with the exception of 11, seven of whom were Negroes, two Mexicans and two American Indians. Their age averaged 23.5 years with a range from 16 to 42. Two hundred and fifty-five (24 per cent) were multigravidas and 803 primigravidas. Of the former number, 217 (20.5 per cent) were parous, having borne one to five children each. Thirty of these, also, had had one to three abortions each. Among the remaining 38 women, 35 had previously lost one to three pregnancies in the first trimester. Two others had had one ectopic and one abortion each while a third had produced only one ectopic. Incidentally, the latter had a second tubal gestation while under our care.

Ninety-eight and one-tenths per cent (1,038 cases) of the patients were under observation to the end of the third month of pregnancy while 91.5 per cent (968 cases) were followed beyond the fourth month. All abortions seen, occurred before the end of the third month with the exception of eight.

During the period of scientific scrutiny, a diagnosis of abortion was made and proved anatomically 123 times or an incidence of 11.6 per cent. Three individuals were seen through two each. Of the 123, 23

*Six weeks before airplane service was opened for civilians, but none of the individuals in this study traveled by that route.

were dropped from the study for three reasons: (1) there was no information on travel for 20; (2) two were criminally induced; and (3) one was a therapeutic measure done because of hypertensive cardiovascular disease. None of the last three traveled. Thus, for purposes of a comparative study 100 untimely births were obtained. Of this number, 32 were from multigravidas, 12 of whom had never given birth to a viable infant.

The 20 expectant mothers excluded for reason of no travel data were among the first 223 women seen before information was gathered. Left were 835 for whom complete material was collected for 446. Three hundred and ten of the remaining 389 were under surveillance beyond the first four months of pregnancy. There was no report of vaginal bleeding or abdominal cramps from this group. From knowledge gained through survey of the personnel turnover at this activity from month to month, there was calculated to be 200 of the 310 that did not journey and 110 who did. The distances covered by the latter are not available, but it seems justifiable to include them to evaluate the final incidence of abortions within each series and to eliminate the factor of selection as much as possible. It can be safely said that the travelers passed over at least 170 miles one way. In the final analyses there were 289 travelers and 467 nonjourney women for the first 16 weeks under study.

Among the 446 women with complete data, 215 took no trips, 179 transgressed 170 to 6,000 miles each in a continuous tour by bus and/or car and/or train before the end of the fourth month, and 52 others covered 170 to 4,000 miles each after this period of time. Repeated trips averaging 1,200 miles were again made by 20 of the 179 patients after the fourth month. The distribution by state, age of the patients, blood counts and body weights were approximately equal for the different groups.

The abortions predominated in the second month (51 cases) with 41 in the third and 8 in the fourth. The clinico-anatomical classification is shown in Table I.

TABLE I. CLASSIFICATION OF 100 ABORTIONS AT THE TIME OF ADMISSION TO THE HOSPITAL ON ANATOMIC BASIS

| CLASSIFICATION | NO. CASES |
|----------------|-----------|
| Threatened | 63 |
| Incomplete | 28 |
| Complete | 2 |
| Inevitable | 2 |
| Septic | 2 |
| Missed | 2 |
| Criminal* | 1 |
| Total | 100 |

*This patient was seen before and after having consulted an abortionist. She traveled 1,800 miles without difficulty before the criminal procedure was performed.

Excluding the criminal abortion, the clinical symptoms and signs were vaginal spotting or gush of blood in 91 instances and cramps or acute lower abdominal pain in the other eight for the onset. Certain diseases and traumatic factors were encountered in 19 persons. Pregnancy complicated hypothyroidism twice, hemolytic icterus and pernicious anemia once each. All but one patient, a hypothyroid, lost the fetus.

Bleeding followed bimanual examination in two instances. In one, it was felt trauma was not sufficient to initiate the onset while the other was equivocal. In the latter, an outside doctor had tried to convert a uterus lying posterior, to an anterior position by pelvic manipulation. Both pregnancies were wasted.

Thirteen individuals had bleeding begin a few minutes to 24 hours after coitus. Four of these aborted while the other nine were only threatened. Nine of the total were seen 12 to 48 hours after the discharge appeared. None had any lesion of the cervix, vagina, urethra or rectum to account for the abnormalities. Afterwards, when they reported for examination, dark blood was visible in the cervical os of eight. The untimely births came from this number. The proximity of the time of the trauma with the period of onset of bleeding suggests that coitus might have been predisposal to the pathologic change.

Of the 19 women discussed above only three had traveled. More will be said about them subsequently.

Consideration may now be given to the problem of travel and abortion. Of the 289 travelers, who toured before the end of the fourth month, 16 or 5.6 per cent had untimely births as contrasted to 84 or 17.9 per cent occurring among the control or sedentary series. Based on the 179 protocols, where the distances covered were known definitely (Table II), 46 (25.7 per cent) were multigravidas and 37 (20.6 per cent) parous. These figures correspond favorably with the percentages for the entire clientele. Of the 16 journey women having abortal

TABLE II. MILES TRAVELED DURING THE FIRST FOUR MONTHS OF PREGNANCY FOR 179* PATIENTS; ABORTIONS OCCURRING WITHIN THAT PERIOD OF TIME

| TOTAL TRIPS | MILES TRAVELED | TOURS ACCORDING TO THE MONTH OF GESTATION | | ABORTIONS | | |
|-------------|------------------|---|-------|-----------|--|--------------------------------|
| | | NO. CASES | MONTH | NO. CASES | CLASSIFICATION | NO. SALVAGED |
| 1 | 25 by motorcycle | 1 | 2 | 1 | Incomplete | Wasted |
| | | 16 | 2 | 1 | Incomplete | Lost |
| 62 | 170 to 500 | 25 | 3 | 3 | Threatened-2 Incomplete-1 | Saved-1; lost-1 Wasted |
| | | 21 | 4 | 1 | Threatened | Lost |
| | | 2 | 2 | 1 | Complete-1 | Wasted |
| 10 | 500 to 1,000 | 5 | 3 | | | |
| | | 3 | 4 | | | |
| 89 | 1,000 to 2,000 | 36 | 2 | 5 | Threatened-2 Incomplete-2 Inevitable-1 | Four wasted or lost; one saved |
| | | 22 | 3 | | | |
| | | 31 | 4 | 2 | Threatened-2 | Two saved |
| 37 | 2,000 to 4,000 | 10 | 2 | 2 | Threatened-1 Complete-1 | Saved Wasted |
| | | 12 | 3 | | | |
| | | 15 | 4 | | | |
| 1 | over 6,000 | 1 | 2 | | | |
| 200 total | | 200 | | 16 | 16 | Five saved; 11 lost or wasted |

*The journeys of 178 patients included the 127 mile stretch over the keys by bus or car. Of the total 200 trips, one was made by 146 women, two by 21 others and three by the remaining four.

difficulties, seven were parous and one other gravid previously. The remaining eight were primigravidas.

Only one patient had a bloody vaginal discharge during transit over a 1,700 mile course, 1,530 by train and 170 by bus. The case was classed as threatened. Two others began bleeding 6 to 12 hours, respectively, after a ride of 170 miles in a car. Subsequently one person put on an aerobic dance in a U.S.O. show. It is probable the athletic performance was the more important of the two factors under consideration as predisposing to the interruption of the pregnancy. Both cases were admitted as incomplete abortions. A fourth woman had an acute attack of lower abdominal cramps and gush of blood shortly after a bumpy motorcycle ride. This was also entered as incomplete. The second day after reaching their destination, following in order, a 340, 1,000, 1,800 and 2,000 mile tour, four expectant mothers developed vaginal bleeding. Two eventually went to term while the other two were wasted. Seven patients began losing blood seven to ten days after covering 300 to 4,000 miles each. Two of these gestations were salvaged. The sixteenth case began to have profuse serosanguineous discharge 14 days after a 1,700 mile journey by car was begun and 9 days after it was completed. The Friedman test had been reported as "negative for pregnancy" when the trek was started. However, examination at this end of the course revealed a full two months' gestation. It was eventually lost.

Assuming that travel predisposed to abortion, it is unlikely that any effect could be expected in the last eight cases cited above for the reason the time of the journeys antedated the pathologic change too long, unless consideration of Streeter's work serves as an explanation. He found degenerative changes began often one to six weeks before the actual evacuation of the uterus occurred.¹ It should be stated that abortal signs appeared in three of the eight, 12 to 24 hours after intercourse.

Neither the distances covered and the method of travel employed nor the time of the month at which a journey was taken revealed any significant differences in the incidence of abortion. The 72 women, 20 of whom had also toured before the end of the fourth month, showed no evidence of miscarriage or premature labor on migrating from 170 to 4,000 miles each subsequent to the period stated.

Comment

Up to the present time, statements exist in the literature about cautioning pregnant patients against travel, but in so far as clinical data are concerned, material to substantiate the contention is *nil*. Obstetricians and gynecologists differ in their opinion regarding the advisability of traveling. Some believe any form of journey, short or long, involves risks.^{2, 3} This idea rests on one or both of two premises: one, that riding may stimulate the neuromuscular mechanism to initiate uterine contractions to the point of threatening an abortion. The other entails the individual finding herself in a situation where treatment for a catastrophe is not easily obtained. Of the two factors, the first appears equivocal and from the study presented it becomes more so.

Formerly, when women became pregnant, the majority stayed near home and abstained from taking extended trips. As a result, no one

physician or clinic was apt to have the opportunity of reviewing the results of travel on the incidence of abortion in a relatively large number of cases. And, today means of transportation are so modernized that they do not lend themselves well to evaluate the abnormalities, if any, produced by rough riding.

Probably one of the largest collection of figures available on the transfer of pregnant women over considerable distances are to be found at the University of Iowa where over 17,000 parturients have been delivered between July 1, 1926 and January 1, 1944 and where the majority have been brought by ambulance from all parts of the State of Iowa—the greatest mileage is 350—in the last trimester. Transportation, however, has been conducted largely over well-paved roads. Impressions of the writer gained at this institution never revealed any significant predisposition to the onset of labor or premature birth. Yet this series does not suffice as a comparison for the subject at hand. Here, the problem involves the first four months of gestation when the choriodecidual relationships are supposedly unstable. Spontaneous abortion implicates in most instances a dysfunction lying outside the fetus and possibly outside the ovum. There is reason to believe this is hormonal in nature.⁴ Disturbance of an extrinsic, traumatic nature to be effective would necessitate interference with the blood supply to the nidatory site, damage to the membranes, serious injury to the young corpus luteum or activation of the neuromuscular mechanism of uterine evacuation by local irritation or by cerebral abnormalities.⁵ Of the factors mentioned, the last one would appear to be the logical cause, but clinical results offer little, if any, confirmation that there is a consequence from the usual procedure of transport.

A notation is required as to why more abortions were found among the sedentary group than among the travelers. It is difficult to say. Nevertheless, three reasons are given: the number of cases available was statistically too small. This was inferred in the introduction. Second, patients who would have left this area before or who would have come to this section in the first four months of their pregnancy were prevented from doing so by reason of the actual occurrence of a pathologic birth. Third, the economic and gravid factors undoubtedly played a part in selection. Mothers with children could not come to the islet as readily as women without offspring. But the final results warrant the conclusion that travel by car or bus over the rough stretch of highway covering the keys and over modern roads and/or train in the states did not increase the incidence of abortion among travelers as opposed to nonjourneying women. It is doubted that transportation alone predisposed to abortion except in one case where the woman had ridden a motorcycle a few hours previously. Even here the cause and effect connection is equivocal. On the other hand the physical activity concomitant with riding is conceded to have facilitated interruption of an early gestation where intrinsic and other extrinsic factors were already

in action. In general, it appears that the principal argument against traveling entails the necessity of an expectant mother being cared for medically wherever trouble may arise and with such resources as are present. For this reason, pregnant women must assume the responsibility to journey long distances.

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SOME ACQUIRED BONY ABNORMALITIES INFLUENCING THE CONDUCT OF LABOR*

With Reports of Recent Cases

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MUCH has been written about labor in women with abnormal bony pelves. Most of these pelves are congenitally abnormal. In this paper, however, we are concerned only with those abnormalities which have been acquired, due to either trauma, specific disease, or to neoplasms. It must be kept in mind that some of these conditions can affect the bony pelvis directly. Others, in the course of time, can exert an indirect effect through abnormality of the spine or lower extremities. Schauta, Litzmann, Williams¹ and more recently Caldwell and Moloy² have included acquired abnormalities in their classifications of the pelves. For purposes of reference the following simplified classification is suggested.

ACQUIRED BONY ABNORMALITIES INFLUENCING THE CONDUCT OF LABOR

| | | |
|--|-----------------|---------------------|
| I. As a result of Trauma A. Fractures B. Dislocations | Pelvis | Pubis |
| | | Ischium |
| II. As a result of Specific Disease A. Bacterial Infection {Tuberculosis Osteomyelitis B. Dietary Deficiency Rickets and Osteomalacia C. Miscellaneous Diseases of Nervous System (Polio) Osteoarthritis Acromegaly Paget's, Multiple myeloma, Syphilis, Echinococcus Cysts, etc. | Spine | Ilium |
| | | Sacrum |
| III. As a result of Neoplastic Disease A. Benign B. Malignant | Lower Extremity | Coccyx |
| | | Dorsal Lumbo-sacral |
| | | Upper Femur Hip |

Recently we have had experience with cases in each of these main categories which will serve as examples.

Trauma

Until the advent of fast motor travel in recent years, the incidence of pelvic fracture as a complication of labor was comparatively rare. B. C. Hirst³ in the original edition of his *Textbook of Obstetrics*, published

*Read at a meeting of the Philadelphia Obstetrical Society, December 2, 1943.

in 1898, states: "Only 0.8 per cent of all fractures involve the pelvis. When one considers that almost all grave injuries of the pelvis end fatally, the rarity of a pelvic deformity dependent upon united fractures of a pelvic bone in a woman of childbearing age may be appreciated."

In recent years, however, the incidence of pelvic fracture has greatly increased. At the Kensington Hospital for Women, three such cases have been encountered by us in the past 28 months. It was surprising, therefore, to find so few cases reported in the English language. Standard textbooks on obstetrics briefly mention the subject, or ignore it entirely. The 1941 edition of Williams' *Obstetrics*⁴ gives in essence the same material that was included in B. C. Hirst's original edition in 1898.

There are a number of factors which recently have influenced the incidence of pelvic fracture in women of childbearing age.⁵ The widespread use of the automobile, and the ever increasing speed of these vehicles have been a prime factor. Fractures of all kinds have become more prevalent and fractures of the pelvis have become relatively more common than ever before. They are quoted by Kellogg Speed⁶ as comprising 3 per cent of all fractures. In former years, the vast majority of fractures of the pelvis occurred in men, but in the most recent series of cases from 44 per cent to 50 per cent⁷ of these injuries occurred in women. The female pelvis is known to be more frail than that of the male, and so we may expect to see an ever increasing number of pelvic fractures, not only because of automobile travel, but also because women are filling men's jobs in industry now more than ever before. Another important factor is the decreased mortality in cases of pelvic fracture. Formerly up to 50 per cent of the patients died. Recently, Eliason and Johnson⁷ reported but five deaths in a series of sixty cases of acute fracture of the pelvis. Sever⁸ reported but one death in his series of fifty-one cases.

Fractures may occur in almost any portion of the pelvis. Eighty per cent of the cases have multiple fractures. Common sites are the rami of the pubis and ischium, and the alae of the ilium. Fractures of the pelvis are usually the result of severe impact. Eighty per cent now occur in automobile accidents. The injury commonly occurs as the result of the passenger in the rear seat of an automobile being thrown forcibly against the side of the car. Being thrown from a car, or crushing accidents are not unusual happenings. Occasionally, however, simply falling on an icy pavement, or tripping over a rug may cause pelvic fracture in women.

From the obstetric standpoint, the lateral crushing fractures are the most important because greater distortion of the pelvic inlet is likely to result. Fracture of the descending ramus of the pubis is of serious import if there is a great deal of displacement because the outlet of the pelvis may be encroached upon. A severe fracture about the symphysis pubis with separation or displacement is dangerous because of the pos-

sibility of injury to the urethra or bladder upon descent of the presenting part, even though no such injury had been evident at the time of the fracture.

These facts are extremely important from the medicolegal point of view. As these accidents increase in young women, the obstetrician will be called upon more frequently to give testimony in court. In these instances, it would be well to bear in mind the favorable effect that is exerted by the lapse of time. After a few years have passed, some of the most severe cases of pelvic fracture are surprisingly free of excessive callous formation or severe pelvic deformity. Quite often nature helps to compensate for these deformities by bringing about premature labor or producing a small baby. In giving expert testimony in these cases, we should determine if possible the type of pelvis present before the fracture occurred. A fracture can occur in a justo-minor or funnel-type pelvis just as well as it can in the gynecoid type. To remember this might save embarrassment during cross examination.

The conduct of labor in cases with fracture of the pelvis depends upon the degree of distortion present, the size of the baby, and how recently the fracture occurred. Elective cesarean section should be done where there has been a severe lateral crushing injury causing obvious obstruction. This operation should also be done in cases of marked displacement in the region of the symphysis pubis where injury could occur to the urethra or bladder. This also is probably the best procedure in those cases with acute fracture of the pelvis with displacement, if labor starts. In borderline cases of inlet contraction, a trial of labor can always be employed to see if engagement occurs. It is safe to say, however, that most cases will deliver vaginally without undue difficulty. It is often wise to terminate the second stage of labor early with forceps in order to lessen the strain on the affected region.

The dislocation of joints due to trauma sometimes may cause concern. Dislocation of the head of the femur usually causes no marked pelvic deformity even though it be congenital. In case of bilateral subluxation, the heads of the femora may project into the pelvis through the sciatic notches when the patient is put in the normal abduction position for labor. This causes marked bilateral narrowing of the pelvis. Verning⁹ has delivered sixteen such cases normally simply by abandoning the obstetric position and adducting the legs.

Forward displacements of the coccyx with ankylosis of the sacrococcygeal joint due to an old injury are met with occasionally. Hirst and Wachs¹⁰ have summarized this condition well. While this may cause dystocia at the pelvic outlet, it usually is not serious. The delivery is ordinarily completed with low forceps and the obstructing coccyx forcibly pushed backward. It is not common for the mother to have residual symptoms after this procedure, although occasionally the coccyx must be removed surgically.

Specific Disease

The second category in our classification includes those abnormalities caused by a specific disease. These cases are uncommon; those due to bacteria, especially tuberculosis, are seen most frequently. The rachitic pelvis was at one time a rather common cause of pelvic dystocia. Fortunately, at least in most parts of this country, this sequela of dietary deficiency is now seldom seen. Under the miscellaneous group of bone diseases which includes syphilis, Paget's disease, multiple myeloma and such entities, the course of labor is seldom affected. Occasionally, echinococcus cysts of the pelvic ring will cause dystocia. De Sa's¹¹ case of bizarre crippling due to arthritis deformans and Bringle's¹² interesting case of acromegaly, both delivered their offspring spontaneously. In cases of old poliomyelitis with unilateral lameness, there is sometimes a slight obliquity of the pelvis, but never as severe as in those cases in which the lameness is due to hip disease.

Under bacterial disease, osteomyelitis of the pelvic bones has been described in detail in Wilensky's¹³ excellent monograph. In our experience, this disease has not caused severe pelvic dystocia. We, therefore, direct our attention to tuberculosis since we recently have had experience with a case of low Pott's disease and two cases of tuberculous hip joint disease.

Before the tuberculin testing of cattle, these complications were more common. Pott's disease, causing kyphotic pelvis, is commonly quoted as occurring once in every six thousand labors. When kyphosis occurs in the dorsal region, there is usually a compensatory lordosis, so that the pelvis itself is not greatly affected. However, the gibbus or hump may be situated in the lumbar or sacral region. Generally speaking, the lower the gibbus, the greater the pelvic deformity, although the greatest deformity becomes manifest when the kyphosis is situated at the lumbosacral junction in the region of the promontory of the sacrum.

A typical kyphotic pelvis¹⁴ is characterized by an elongated conjugata vera and a contracted outlet. This is brought about by the fact that the body weight transmitted to the lumbosacral hump is directed both downward and backward. This latter force draws the promontory of the sacrum backward and upward thus increasing the conjugata vera. When this occurs, the posterior extremities of the innominate bones are pushed apart rotating their upper portions outward and their lower portions inward. This causes a transverse contraction of the outlet by bringing the ischial spines and tuberosities closer together. As the upper portion of the sacrum is rotated backward its lower portion is pushed forward thus narrowing the posterior sagittal diameter of the outlet. External measurements of a kyphotic pelvis reveal the distance between the iliac crests to be equal to, or greater than, that between the two trochanters. The diagonal conjugate is deep. The bi-ischial is small as is also the posterior sagittal measurement.

When labor starts, the engagement of the presenting part may be interfered with because the uterus many times inclines forward due to the fact that the abdominal cavity is shortened in a low kyphosis. This usually may be remedied by the application of a tight abdominal binder. Ordinarily, however, no great difficulty is met with until the presenting part reaches the region of the ischial spines. If the sum of the biischial and posterior sagittal measurements equals fifteen cm. or more, no great difficulty in performing a vaginal delivery need be anticipated. If the sum of these two measurements is less than 15 cm. and a good-sized living baby is present, suprapubic delivery is the procedure of choice.

Tuberculous coxitis when it occurs in early life nearly always causes an obliquely contracted pelvis.¹¹ The distortion is almost always on the healthy side. The diseased leg is shortened so that in walking the body weight is transmitted in great part to the well leg. This tends to flatten the iliopectineal line and the sacrum is rotated to some degree about its vertical axis, so that its anterior surface looks toward the well side. The pelvis is affected throughout from the inlet to the outlet. X-ray pelvimetry is of prime importance in evaluating the prognosis of labor in these patients. If it appears probable after such a study that engagement will not occur, cesarean section should be performed before the onset of labor. Otherwise, a trial of labor should be utilized to see if engagement takes place. The majority of cases will deliver spontaneously. Some authorities feel that in cases where the ankylosed leg assumes an awkward position and indications for a forceps delivery exist, internal podalic version gives better results because of difficulty in applying the forceps.

Case Reports

I. Fractured Pelvis

CASE 1.—Mrs. M. W. This 31-year-old gravida i, para 0 was involved in a serious automobile accident at eight months' gestation. She suffered a double fracture of the horizontal ramus of the left pubic bone (Fig. 1). She was treated for a month with bed rest on a Bradford frame. At term, the head failed to engage, and because of the recent pelvic fracture, a cesarean section was done and a living seven-and-a-half-pound infant delivered. A year later, this patient again became pregnant. At eight months' gestation, an x-ray of the pelvis (Fig. 2) revealed complete healing of the old pelvic fracture without significant deformity. She was allowed to go into labor spontaneously at term, and was delivered after a short uneventful labor with outlet forceps of a living eight-pound child. Her puerperium was uneventful and she now is enjoying normal health.

CASE 2.—Mrs. R. W. This 28-year-old gravida iv slipped and fell upon an icy pavement at eight and a half months' gestation. She was unable to walk, so was taken to the hospital where an x-ray revealed a linear fracture of the right pubic bone extending from the symphysis pubis to the obturator foramen. There was no displacement. The patient was treated with simple bed rest. After eight days, she went

into labor spontaneously and was delivered of a normal full-term baby eight hours later with the aid of outlet forceps. The puerperium was normal. Two weeks following delivery, another x-ray showed no change from the previous film except for the presence of beginning of callous formation. The patient was then able to walk and returned to her home a few days later. At the present time, she is again pregnant and has no symptoms whatsoever.

CASE 3.—Mrs. M. D., 23-year-old gravida i, para 0, who had been in a serious automobile accident five years previously. At that time, she sustained multiple fractures of the pelvis with displacement of fragments of the rami of the pubes and ischii. The sacrum was also fractured and the bladder punctured. She visited one of us when she was three months pregnant. X-rays were taken (Fig. 3) which showed marked distortion of the pelvic inlet due to old united fractures, espe-



Fig. 1.

Fig. 1.—Patient at 8 months' gestation with acute fracture of the horizontal ramus of the left pubic bone with some displacement. Delivered by cesarean section.



Fig. 2.

Fig. 2.—Same patient twenty months later with her second pregnancy. Note how the contour of the pelvis has been almost completely restored. Delivered vaginally.

cially of the left pubic bone. The left obturator foramen showed 75 per cent diminution in its anteroposterior diameter. The body of the left pubic bone was seen to be impacted into the superior and inferior rami causing great narrowing of the forepelvis, although the internal conjugate measurement was 10 cm. and the greatest transverse diameter was 10.4 cm. The patient went through a normal prenatal course without change in this picture as shown by repeated x-rays. Because of the previous bladder injury and the obvious pelvic distortion, it was decided that an elective cesarean section would be the wisest means of delivery. She was admitted to the hospital a week before the estimated date of confinement, but went into labor early in the morning of the day she was to be sectioned. After an easy labor of five hours' duration, she spontaneously delivered a living six-and-a-half-pound child. The patient had an uneventful puerperium. X-rays taken ten days after delivery showed no change whatever from the previous films.

II. Cases of Tuberculous Hip Disease

CASE 4.—Mrs. D. B. A case of a 20-year-old gravida iii who had had two previous cesarean sections before her first visit to us. She gave a history of hip disease since the age of ten years, and had walked with a limp ever since. X-ray taken of the pelvis showed a characteristic tilting but no deformity of the pelvic ring. Information was obtained that the previous cesarean sections had been done because of increasing hip pain during the last several weeks of pregnancy. It was obvious, however, from both clinical and x-ray measurements that the pelvis was ample in size. Because of the previous sections and the severe pain that always occurred near term, another cesarean section was done and a Pomeroy sterilization carried out.



Fig. 3.—Multiple fractures of pelvis and punctured bladder sustained five years before first pregnancy. Note the contracted forepelvis and bizarre contour of the left pubic bone and obturator foramen. Delivered vaginally. This picture was taken at three months' gestation.

CASE 5.—Mrs. N. A case of a 29-year-old gravida i, para 0, who had tuberculous coxitis when a child. She then developed an ankylosed hip with marked tilting of the pelvis. X-rays revealed only a slight oblique contraction of the pelvic inlet. She was delivered without complication of an eight-pound baby with outlet forceps. A year later, she spontaneously delivered a nine-and-a-half-pound infant. The only unusual procedure that had to be used in delivering this patient was the pulling of her involved leg laterally with a sheet. This had to be done in order to give room for delivery because the affected hip was ankylosed and fixed in adduction.

III. Kyphotic Pelvis

CASE 6.—Mrs. E. B. A case of a 28-year-old gravida i, para 0 who gave a history of having had trouble with her spine since she was six years old. She had subsequently had bilateral psoas abscesses which drained for years but finally closed up. Physical examination revealed

a gibbus in the lumbosacral region. The pelvic inlet was apparently horizontal and the thoracic cage rested upon the alae of the ilii. The pelvic measurements were:

Intraspinous 26 cm.
 Intercrestal 29 cm.
 Intertrochanteric 28 cm.
 Diagonal conjugate 14 cm.
 Biischial 9.5 cm.



Fig. 4.—Kyphotic pelvis with gibbus in lumbosacral region. This film was taken at term. Note the engaged head with the body obliquely forward; the latter is due to the great shortening of the abdominal cavity. The application of a tight abdominal binder helped to correct this. Delivered vaginally with midforceps.

X-ray showed the upper portion of the sacrum to be pushed posteriorly and its lower portion to be pushed forward. Apparently, the patient would have normally had a very spacious pelvis and even though the inlet was now dilated, the outlet, while it was somewhat contracted, seemed ample for the passage of a normal-sized baby. Therefore, she was allowed to go to term and have spontaneous labor. At this time she had an extremely pendulous abdomen because of the shortness of her abdominal cavity. (Fig. 4). An abdominal binder was applied. Labor progressed normally until the vertex reached mid-pelvis where it became arrested. She was delivered after seventeen hours of labor with midforceps of an eight-pound three-ounce infant. The puerperium was normal.

Neoplasms

Our third category embraces abnormalities due to neoplasms. These are unusual but interesting. Neoplasms of the spine ordinarily cause no difficulty in pregnancy unless they involve the sacrococcygeal region and there are but few cases of this sort reported. Those affecting the femur may make adjustments necessary in the conduct of labor. There are very few cases reported in the literature¹⁵ of primary sarcoma of the upper femur associated with pregnancy. Such a case (Fig. 5) is now under the observation of one of the authors and will be reported later.

Tumors of the pelvic girdle can, however, cause serious dystocia.¹⁶ Of the malignant tumors, 5 per cent of osteogenic sarcomas, which is a neoplasm of young people, occur in pelvic bones, according to Francisco.¹⁷ Metastatic carcinoma frequently involves the pelvis, but usually is seen in older individuals. The benign neoplasms are the most common. These are usually bony exostoses which may be found over the iliopectineal eminences, the crests of the pubis, or over the pelvic joints. Like the enchondromas, which grow rapidly during pregnancy, they often cause serious obstruction to labor. These usually are symptomless, and therefore often are not recognized until they have arrested the progress of labor. In one series of thirty cases quoted by Williams,⁴ twenty-one cesarean sections and three destructive operations upon the fetus were necessary. While such tumors are seldom encountered, the obstetrician should have knowledge of them and keep in mind their possible presence in vague cases of dystocia.



Fig. 5.—Sarcoma of upper right femur complicating pregnancy.

Summary

1. A simplified classification of acquired bony pelvis abnormalities and their effect upon the conduct of labor has been presented and discussed.

2. Cases recently seen have been presented as examples of each main category.

3. It is our opinion that more emphasis in teaching should be placed upon acquired anomalies of the pelvis, especially pertaining to fractures of the pelvis which are rapidly increasing in frequency.

4. After study of these acquired anomalies, it is found that operative delivery in such cases should be the exception rather than the rule.

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5501 GREENE STREET

THE CHARACTER OF VAGINAL DELIVERY FOLLOWING CESAREAN SECTION

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THERE is a difference of opinion concerning the nature of the first vaginal delivery occurring in a patient who has had a cesarean section. The question is whether or not the labor is comparable to that of a multipara or a primipara, especially in regard to the total duration of labor and the course of the first stage of labor.

This study comprises a review of 34,356 pregnancies occurring in the Woman's Clinic of the New York Hospital from September 1, 1932 to December 31, 1943. Of this total, 496 patients had a previous cesarean section, an incidence of 1.44 per cent. In this group 109 patients (an incidence of 21.97 per cent) were delivered of a full-term or premature infant per vaginam without ever having had a vaginal delivery preceding the first cesarean section.

The histories of these 109 patients were studied in detail and divided into three groups in order to compare the duration of the stages of labor. The first group consists of the total 109 cases having a vaginal delivery following a cesarean section for the first pregnancy; the second consists of 39 of these cases in which a cesarean section had been performed for an indication other than contracted pelvis, and in which there had been some labor; the third group deals with 36 cases in which an elective cesarean section had been done with no labor prior to the operation.

Table I shows the average duration of labor in hours for each of the groups:

TABLE I

| | GROUPS | | |
|--|----------|----------|----------|
| | I | II | III |
| NUMBER OF CASES | 109 | 39 | 36 |
| Hours of labor before cesarean section | 19 | 11 57/60 | 0 |
| Vaginal delivery | | | |
| First stage of labor | 15 14/60 | 15 27/60 | 16 33/60 |
| Second stage of labor | 54/60 | 45/60 | 56/60 |
| Total labor | 16 19/60 | 16 20/60 | 17 46/60 |

The widely accepted average duration of labor in primiparas is 18 hours and in multiparas 12 hours.¹

Many of the sections in Group I were done for contracted pelvis, a factor which would tend to increase the duration of labor in subsequent pregnancies. The average duration of labor in this group was 16 hours and 19 minutes. In Group II, in which the factor of contracted pelvis had been eliminated, the duration of labor averaged 16 hours, 20 minutes, the duration stated for the labor of primiparas with normal pelvis.² It is seen that in the 36 patients of Group III in whom there had been no previous labor, the average duration of the labor of the vaginal delivery was the same as that stated for primiparas.

McLane is in agreement with these conclusions. In a study of 38 cases of vaginal delivery following cesarean section, he concludes that since most were para i the average labor of 15 hours, 36 minutes, is evidence in favor of the primiparous nature of labor following primary cesarean section.³

It is probable that labor preceding a primary cesarean section may alter the cervix, tending to produce a multiparous behavior observed at subsequent labors, but this is not seen if no labor has preceded the section.

The second stage of labor is about the same for all three groups, which could be explained by the fact that forceps were used frequently to terminate the second stage of labor, the indication being a previous cesarean section. Table II shows the incidence of forceps and episiotomies in the groups studied.

TABLE II

| | GROUPS | | |
|------------|-------------|-------------|-------------|
| | I | II | III |
| Forceps | 56 per cent | 46 per cent | 61 per cent |
| Episiotomy | 87 per cent | 84 per cent | 91 per cent |

The incidence of forceps deliveries in this clinic as a whole is 13.06 per cent, and of episiotomy 50.86 per cent. There was no instance of ruptured uterus in the 109 cases of vaginal delivery.

The fetal mortality, including premature, full-term and neonatal deaths, in this series of 109 cases was 5, or 4.6 per cent, as compared with a figure of 3.10 per cent for the whole clinic.

Summary and Conclusions

1. In 34,356 obstetric patients admitted to the New York Hospital, a previous cesarean section had been performed in 496, or 1.44 per cent.

2. Of this group of 496 patients, 109, or 21.97 per cent, were delivered vaginally of a viable infant, without having had a vaginal delivery previous to the cesarean section.

3. The average duration of labor of the first vaginal delivery in a patient who was delivered by cesarean section in her first pregnancy is virtually identical with that in a primipara.

4. In the group of 109 patients with cesarean section followed by vaginal delivery, there was one maternal death, due to cerebral embolism.

5. The fetal mortality in this series was 4.58 per cent.

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SUBCLINICAL POST-PARTUM SALPINGITIS AND ONE-CHILD STERILITY, A PATHOLOGIC STUDY

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ACUTE salpingitis is a recognized sequel of puerperal endometritis, complicating most frequently criminal abortions, to a lesser extent legitimate operative procedures, and occasionally spontaneous term parturition. Curtis¹ summarizes the generally accepted concept of this lesion as follows: "It has long been known that infection which complicates abortion travels through the cellular tissues rather than along the mucous membrane. The tubes, if diseased, present only part of a relatively diffuse process. We have learned that the tubes when involved are usually attacked from without, the infection producing a perisalpingitis with tendency to invasion of the mucosa last, if at all."

The absence of mucosal involvement is emphasized by most authors, who lay stress upon this fortunate circumstance because of the retention of tubal patency subsequent to the lesion.

Some few authors deduce from their clinical experience that the Fallopian mucosa is not spared and that unexpected tubal obstruction, in some patients, may be due to unrecognized post-partum salpingitis. Rubin,² for example, found that of 195 instances of one-child sterility (a few with 2 children) 45 cases (23 per cent) had nonpatent tubes. In these cases no cause of an ascending infection other than the previous pregnancy could be assigned. Holtz³ after examining the problem of one-child sterility concluded, on a purely inductive basis, that such sterility may be due, in some measure, to an ascending salpingitis contracted during parturition, or the puerperium with consequent occlusion of the tubes. DeLee and Greenhill⁴ in a discussion of post-partum sterilization remarked, "There is good reason for believing that infection sometimes invades the tube as it does the uterus after delivery."

An intensive search of the literature failed to reveal any pathologic studies directed toward the solution of the problem presented by such opposed views.

Material

The material for this study consists of bilateral tubal segments removed, in the course of sterilization, from 67 patients. Of this number, 50 were obtained post partum following normal delivery and the remaining 17, used as controls, upon cesarean section cases. The operations were performed between March 11, 1942 and October 21, 1943. In all instances sections of both Fallopian tubes including mucosa were reviewed.

The chief indications for sterilization were, in the order of their frequency: multiparity, severe toxemias of pregnancy, and heart disease.

Of the 50 post-partum patients, 38 were colored and 12 white. In view of the small numbers no attempt was made to segregate the cases by color.

All the patients, with one exception, were operated upon at some time between the second and twelfth post-partum day. The one exception submitted to sterilization on the twenty-fifth post-partum day.

Results

The Fallopian tubes of the 17 control cases (cesarean sections) represent organs not exposed to the puerperium. Since upon microscopic examination all were found normal, the assumption appears warranted that before parturition the tubes are not the site of acute inflammatory changes. It is possible, of course, that vestiges of a salpingitis acquired in an earlier period of life might still be visible; such lesions, however, cannot be confused with those to be described and are therefore not pertinent to this study.

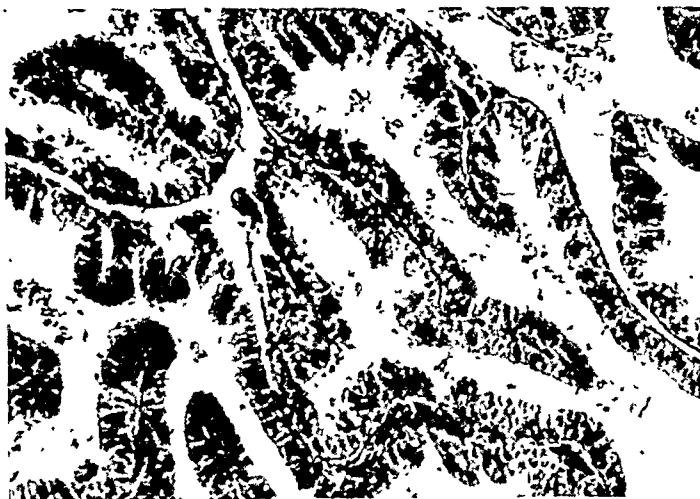


Fig. 1.—Mucosal villi of post-partum Fallopian tube showing normal structure.

Histologic investigation of the sections of the post-partum group revealed that 38 per cent (19 of the 50 cases) were the site of an acute salpingitis. In two instances the inflammation was unilateral, in the remaining 17, bilateral.

The mucosa of the tubes was the stratum most prominently involved. The villi were edematous and infiltrated by polymorphonuclear leucocytes and round cells. In the lumina of most of the organs a small quantity of purulent exudate was present. Nowhere had the inflammation progressed sufficiently to produce accretion of the villi, although in two cases desquamation of the lining epithelium had already made its appearance, a precursor of adhesion formation.

In those tubes which showed the most advanced lesions, aggregates of polymorphonuclear leucocytes were seen in the edematous, hyperplastic muscularis and subserosa. In no case, however, was the peritoneum involved.

Unilateral salpingitis would be difficult to explain had the infection reached the tubes via the lymphatics and blood vessels from the endometrium. The anastomoses of the vessels of the uterus and Fallopian tubes are so abundant that exemption of one tube from the process would appear most unlikely. Extension of the infection by direct extension along the endometrial mucosa to that of the Fallopian tubes could, on the other hand, result in unilateral salpingitis were the lumen of the contralateral side completely blocked. Since in the above two cases the uninvolved tubal segments must be presumed to have been distal to such an assumed obstruction, the surmised block cannot be demonstrated in this material nor, for that matter, in any material other than that obtained by hysterectomy.



Fig. 2.—Edematous mucosal villi of post-partum Fallopian tube infiltrated by polymorphonuclear leucocytes and round cells. Abundant purulent exudate within lumen is characteristic of the more pronounced form of post-partum salpingitis.

The significance of the time interval between delivery and operation in the two groups was investigated. The average interval for those patients free of salpingitis was 5.4 days, for those who developed the lesion, 6.7 days, a difference of 1.3 days.

If it be assumed that a longer interval between delivery and salpingotomy favors the establishment of salpingitis, a comparison of the appropriate subgroups of the two categories should demonstrate a significant difference between them.

Thirteen (42.0 ± 8.8 per cent) of the nonsalpingitis group were operated upon 6 or more days (midvalue of 5.4 and 6.7 days) after delivery. The corresponding number from the salpingitis group was

14 (73.7 ± 13.4 per cent). The difference between these values (31.7 ± 13.4 per cent) is not statistically significant; however, "the magnitude of this difference is such as to suggest that larger groups of data might show significant differences."⁵

Except for two infants of 8 months' gestation among the non-salpingitis group and 1 of 7 months among the other, all offspring were delivered spontaneously and at term. It is therefore apparent that the term of gestation and instrumentation were not factors in the production of post-partum salpingitis.

The entire group of 50 women, notwithstanding the pathologic diagnosis of acute post-partum salpingitis in 19, were considered to be passing through a normal puerperium. Since the inflammation probably spread along the endometrium to the mucosa of the tubes, the assumption that an unrecognized post-partum endometritis existed must be made. Hendry⁶ has demonstrated such a lesion in 10 patients curetted between the fourth and fifth post-partum days, the most constant finding was an extensive infiltration of the endometrium by polymorphonuclear leucocytes.

Franz⁷ first and recently Douglas and Rhees^{8, 9} have reported that during the early puerperium the lochia of a majority of afebrile women contain "potentially pathogenic organisms." Stander¹⁰ states "There is adequate proof in our experience from a bacteriologic and pathologic point of view, that infection with both an inflammatory reaction and bacteria in the tissues may exist in the absence of any febrile manifestations." Harris and Brown¹¹ found in their material at Johns Hopkins Hospital that puerperal infections occur five times more frequently in Negro than in white women. In view of the above, it should not be surprising that in this material (76 per cent colored) the incidence of unrecognized post-partum salpingitis should run as high as 38.0 per cent.

Undoubtedly the greater number of post-partum salpingitides are of little importance so far as the course of the puerperium and the future patency of the tubes are concerned. It is not, however, without the bounds of probability, that in some of these cases the lumina may be so distorted or constricted as to impair the fertility of the patient or even produce complete sterility. Franz⁷ concluded that primipara show approximately a 50 per cent greater incidence of moderate temperature elevations during the puerperium than multipara. Such temperature fluctuations are considered to be evidence of puerperal infections. This would indicate, therefore, that the incidence of post-partum salpingitis, in primipara, may be correspondingly higher than in multipara. Those who suffer changes sufficiently great to reduce their fertility to functional or organic sterility would, of course, never have reason for sterilization, and would as a result escape any possibility of systematic pathologic investigation. With this in mind, Rubin's² discovery of tubal occlusion in 23 per cent of 195 cases of one-child sterility with no apparent cause other than the previous pregnancy should be remembered.

In order to further investigate the etiology of subclinical post-partum salpingitis, a bacteriologic study of a series of Fallopian tubes, similar in all respects to that described above, has been entered upon.

Summary and Conclusions

1. Bilateral tubal segments of 67 patients were histologically examined. Seventeen were removed at term cesarean operation, and 50 at varying intervals during clinically normal puerperia.

2. The 17 cesarean section pairs (controls) showed no pathologic lesions.

3. Of the 50 post-partum pairs, 38 per cent (2 unilateral) were the site of a mild acute salpingitis.

4. In no case was the salpingitis clinically recognized.

5. It is suggested that this hitherto not demonstrated but suspected puerperal salpingitis may in some patients be the cause of tubal obstruction with resultant reduction of fertility, or even sterility.

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INTERSTITIAL PREGNANCY, WITH REPORT OF A CASE OF FULL-TERM GESTATION*

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ECTOPIC pregnancy in the interstitial portion of the tube is especially interesting not only because of its infrequency, but also because of the peculiar hazards and obstetrical problems which it creates. Gestation within the cornual portion of the tube was recognized as an entity about two centuries ago. All cases up to 1893 were recognized on the autopsy table. After rupture the sudden alarming symptoms of shock which intervened were treated expectantly with the resultant 100 per cent mortality.

The year 1893 marked a new era in the treatment of this condition. Traub,¹ operating on a case performed a supravaginal hysterectomy with subsequent recovery. In 1875, Fritz² reported 18 cases in the literature; the first American to report on the above condition. In 1896, Rosenthal³ studied, 1,324 cases of ectopic gestation of all types and found 40 cases of true interstitial pregnancy, an occurrence of 3 per cent. In 1914, Waegeli⁴ made an exhaustive study of the subject. He accepted 53 of the 150 cases cited, and reported 2 additional cases. Until that time, 11 cases were operated upon before rupture. In a series of 1,547 cases of ectopic pregnancy collected by Wynne⁵ from several of the larger clinics, there were 18 cases of interstitial pregnancy, an incidence of 1.16 per cent. The total number of cases of interstitial pregnancy reported by Wynne up to 1917 is 91, of which 21 were unruptured. The decade between 25 to 35 years of age showed the greatest number of cases.

Since 1918, there have been an additional 108 cases reported, bringing the total number of cases of interstitial pregnancy appearing in the literature to 199. This covers the period up to July, 1943.

To be classified as true interstitial pregnancy, the gestation sac must lie within the wall of the uterine cornu between the proximal end of the isthmic portion of the tube and its uterine orifice. In the normal uterus, the interstitial portion of the tube is 1 cm. long with a uterine ostium 1 mm. in diameter. It forms an arc upward and convex. The folds of mucosa in this portion are fewer and not so deep as those of the isthmus.

Morbid anatomy and clinical symptoms are dependent to a great extent upon the site of lodgement and direction of the growth of the ovum. Hypertrophy and hyperplasia of the parenchyma of the uterus

*Presented at a meeting of the Brooklyn Gynecological Society, April 14, 1944.

about the gestation sac, coincident with the development of the sac are the factors which determine the gross appearance of the fundus as well as the relationship of the appendages. If the ovum lodges in the uterine ostium of the tube, development of the sac does not result in marked asymmetry of the fundus during the early weeks. If the sac is near the periphery of the uterus, asymmetry of the fundus is an early sign. Growth of the sac occurs in the direction of least resistance, which may be determined by the thickness of the uterine wall. When asymmetrical development occurs, the diagnosis may be made more easily.

Conditions which may show signs similar to those of interstitial pregnancy, are pregnancy in one horn of a bicornuate uterus, cornual pregnancy, a myoma in one cornu, or unilateral cornual abscess.

Irregular bleeding occurred in nearly two-thirds of Wynne's cases. A persistent amenorrhea occurred in the remainder. The latter symptom is an important factor in the differential diagnosis.

According to Polak,⁶ interstitial pregnancy may terminate in one of the following ways:

1. Death of the ovum.
2. Expulsion of the ovum into the uterus in which case pregnancy may terminate into an abortion or proceed as an intrauterine pregnancy.
3. Rupture into the peritoneal cavity with death of mother from hemorrhage and shock.
4. Rupture into the broad ligament.

Statistics show that the usual time for rupture is during the second and third months. Interstitial pregnancies are very rarely seen after the sixth month. Two cases at almost full term were reported,^{7, 8} in one of which a living infant was delivered. Three cases of full-term interstitial pregnancies are recorded in the literature up to the present time.⁹⁻¹¹ This report is, therefore, the fourth case of full-term unruptured interstitial pregnancy, and is probably the only one which went so far beyond term.

Case Report

G. D., Italian gravida i, 22 years of age entered the Cumberland Hospital on November 8, 1934, with a complaint of an overdue pregnancy and cessation of fetal movements since the first of September, 1934. Her last regular menstrual period was November 23, 1933. Prior to this, her periods had always been regular. She vomited during the early months of her pregnancy. The expected date of confinement was September 1, 1934. During March, 1934, the patient was seized with intermittent abdominal pain and vaginal bleeding which forced her to go to bed. From then on her pregnancy progressed apparently normally. She passed her expected date of confinement without going into labor, but from then on she felt no fetal movements. On October 7, 1934, the patient began to spot, accompanied by occasional cramplike pains. The spotting lasted 3 weeks. Two weeks before admission, the patient was seized with severe, sharp colicky lower abdominal and back pains which

lasted half an hour, not accompanied by nausea or vomiting. There was no vaginal bleeding since one week prior to admission, and no complaint of any headache, dizziness, visual disturbances or epigastric pain.

Her family history and past history were irrelevant.

Physical examination showed a young woman who appeared to be comfortable. The eyes, mouth, throat, neck, heart and lungs were negative. The extremities and reflexes were normal. Abdominal examination showed a symmetrically enlarged ovoid uterus extending from the pelvis to above the umbilicus and into the left upper quadrant, where the head of the fetus could be easily palpated through the abdominal wall because of easily felt overlapping sutures of the skull. No fetal heart was heard. No small parts could be felt.

The patient showed a nulliparous introitus and vagina. The cervix was small, soft and situated high and posteriorly in the vault of the vagina. The external os was closed. Anteriorly to the cervix and just above, about the level of the internal os, a well-rounded, firm and hard mass was felt. The cervix seemed freely movable and also apparently moved independently of the mass. Blood pressure was 124/72.

Urine showed no sugar, albumin or casts. The Friedman test was negative. The blood Wassermann test was negative. P.S.P. test showed 35 per cent excretion after 2 hours. Blood chemistry showed sugar 61.3 mg. per cent, and urea nitrogen 12.1 mg. per cent.

X-ray examination November 9, 1934, showed evidence of a single fetus lying in breech presentation. There was evidence of overlapping of the cranial bones. Subsequent x-ray films on November 22 and November 29 showed no changes in position of the fetus.

Several attempts to induce labor with castor oil and quinine failed. Three weeks after admission, the patient was examined vaginally under anesthesia. The cervix protruded in the posterior vaginal vault about one inch and felt firm. A uterine sound was easily passed through the cervical os for a distance of about 8 cm. and posteriorly to the presenting part of the fetus. The presenting part was easily dislodged from the pelvis and a rounded mass which was thought to be the uterus could be mapped out posteriorly to the presenting part.

On December 1, 1934, a laparotomy was performed. A mass about 14 inches in length and 6 to 7 inches in width was found emanating from the left horn of what was an apparently normal uterus. This mass was composed of a dead fetus within a sac, intimately associated with the left tube, the distal end of which was apparently normal. The left ovary contained small cysts. The right tube and ovary were normal. The uterus was located posteriorly to the sac containing the fetus. There were numerous adhesions of the omentum and the small intestines to the sac. The entire sac and the distal portion of the left tube were removed after separation of the adhesions. After suturing the raw surface of the uterus, the latter was observed to have been reconstructed to its completely normal appearance.

Postoperative Course.—During the first 3 days, the patient developed distention of the abdomen with vomiting on the second day. The patient was lavaged through a Levine tube, and the distention subsided. The patient then made an uneventful recovery, being discharged December 20, nineteen days after the laparotomy.

On January 5, 1935, the patient was seen in the post-partum clinic. She was feeling fine and offered no complaints. The abdominal wound was entirely healed. The cervix was in the axis of the vagina and was not tender. The fundus of the uterus was in the anterior position, in

the midline, normal size and freely movable. Both fornices were free of any induration or masses. Examination two weeks later showed the same findings.

It is of interest to note that about two years later the patient was spontaneously delivered of a full-term living child.

Pathological Report

Specimen consists of an ovoid saclike structure containing a female fetus measuring about 50.8 by 27.9 by 30.5 cm. The resected surface is represented by a triangular area and corresponds to the caudal end of the fetus in the sac.

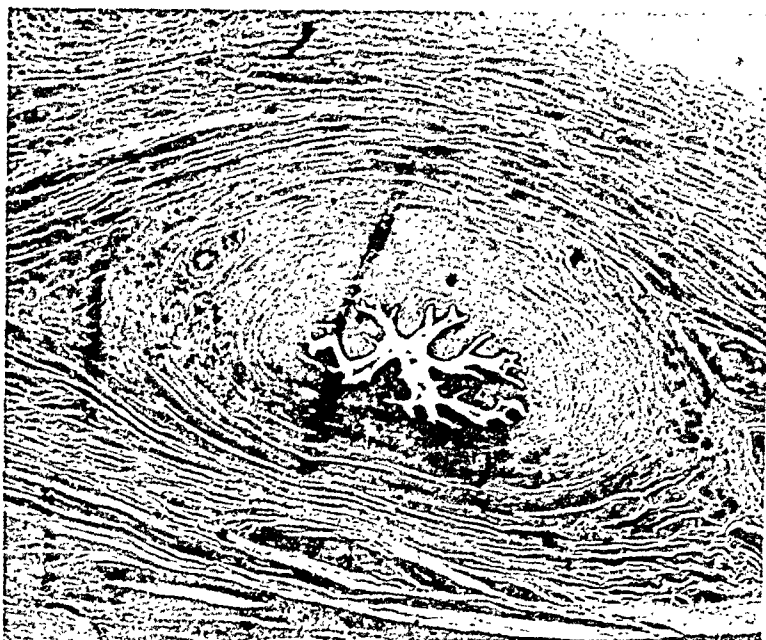


Fig. 1.—Cross section of severed stump of portion of tube showing the characteristic stellate shape of lumen as well as mucosal pattern of this interstitial segment of tube. Note the relatively few folds of the mucosa and the absence of reaction in the mucosa ($\times 35$).

At one angle of the triangular resected area the stump of a tubal structure 1 mm. in diameter, projects from the cut surface. It is the proximal portion of the Fallopian tube. Microscopically, cross sections of this tubal stump show an intact mucosa with rugae characteristic of the interstitial portion of the tube (Fig. 1). There is no decidual reaction in the mucosa, and the inner muscular layer is normal. The outer muscle layer and serosa, however, are both invaded by fetal structure, most of which consists of degenerated placental villi. This layer of tubal wall merges indefinitely with the outer surface of the sac wall and at this level the lumen of the tube is obliterated.

The opposite angle of the triangular area of resection is occupied by a rough brown tissue. Beneath this layer are interlacing bundles of smooth muscle which can be readily identified as myometrium (Fig. 2). Van Giesen stains of this area show extensive fibrous replacement of the myometrium. The rough brown tissue noted in the gross, microscopically, is found to be a small piece of ovarian tissue continuous with a strip of broad ligament.

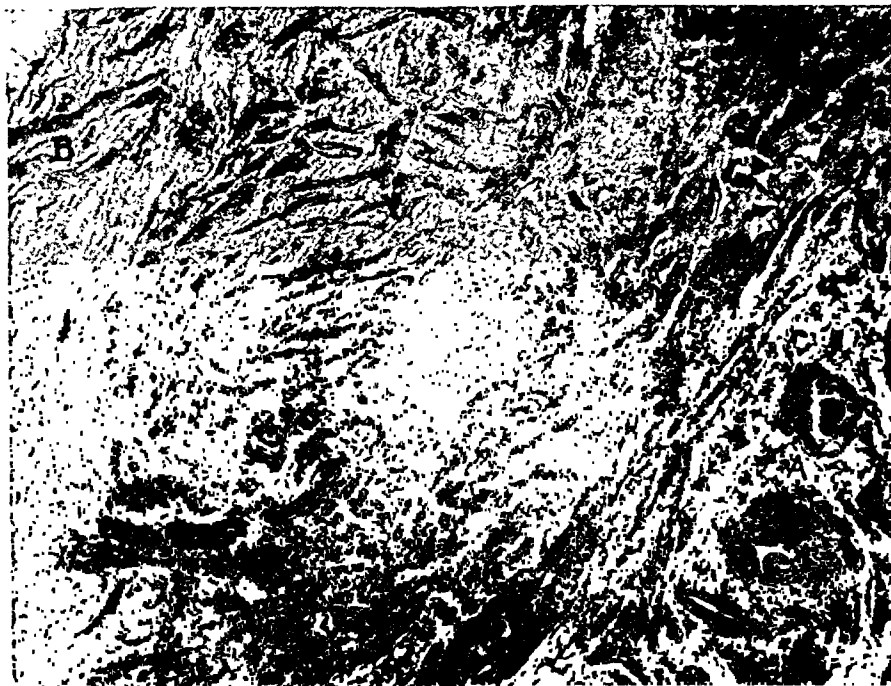


Fig. 2.—Cross section through the triangular area of resection showing denuded myometrium of lateral uterine wall. Note *A*, the cross sections of branches of uterine artery and *B*, the interlacing bundles of myometrium along lateral wall of uterus ($\times 27$).

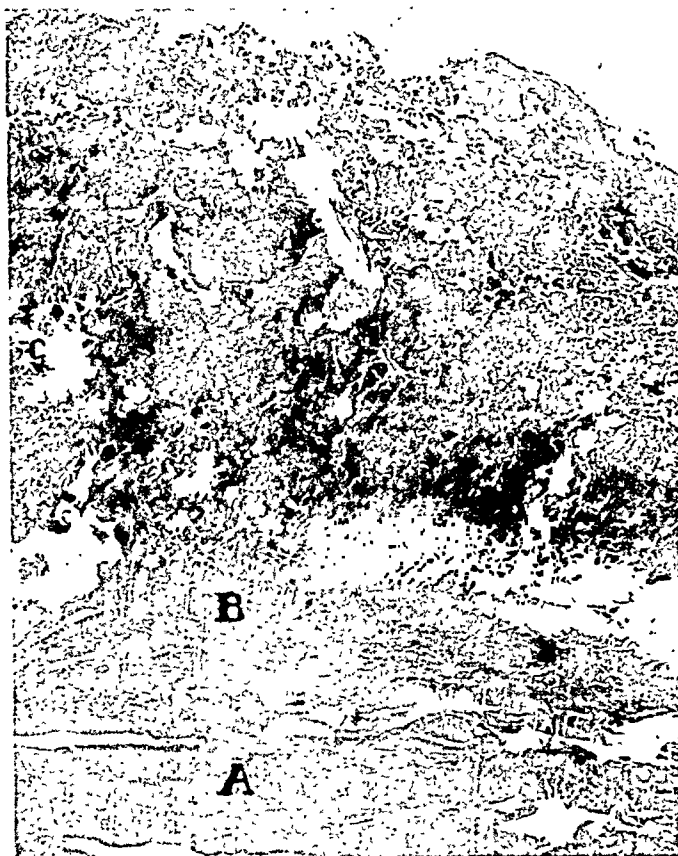


Fig. 3.—Section of the sac wall through the placental attachment showing fibrosed myometrium; *A*, Merging indefinitely with infarcted placenta; *B*, containing abundant calcium deposits; *C*, in the villi ($\times 11$).

The remaining portion of the triangular area of resection (Fig. 3) is composed of numerous large vessels, myometrium and fibrous structure. It merges indefinitely with the deeper, partly calcified placental mass which forms the inner layer of the sac wall. Microscopically, numerous placental villi are found in between bundles of smooth muscle.



Fig. 4.—Fetus and placenta removed from sac. Note short umbilical cord due to loop formed by the latter *J*, midway between fetal *K*, and placental *L*, insertions. Note also macerated condition of the fetus and the extremely large cotyledons *L*, of the placenta containing large infarcts.

On opening the sac, a full-term, partly macerated female fetus is found compressed by the tension of the sac wall, its extremities in complete flexion. The umbilical cord is shortened by an adherent loop (Fig. 4) at a point about midway between its fetal and placental insertions. The placenta is firmly attached to the caudal portion of the sac and the amnion merges indefinitely with the cephalic end where the sac wall becomes extremely thin. The maternal surface of the placenta shows extremely large cotyledons which contain numerous areas of infarction. The fetus is covered with a large amount of lanugo and is fully developed. The skin is discolored gray-brown and shows beginning maceration.

The microscopic sections of the sac wall at the margin of placental attachment show muscle bundles and scant fibrous tissue merging indefinitely with masses of placental tissue much of which is infarcted. Section through the cephalic and thinnest portion of the sac wall (Fig. 5) shows completely hyalinized structure containing fetal masses which

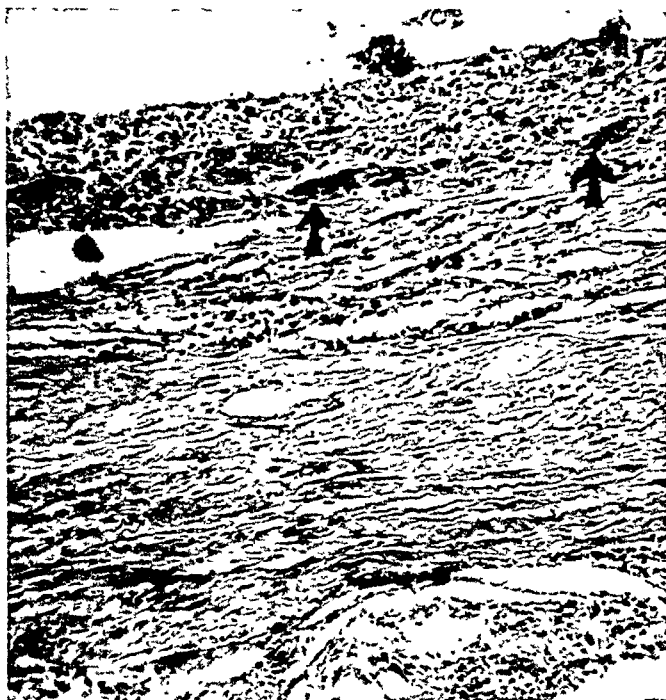


Fig. 5.—High-power magnification through the thinnest portion of the cephalic end of the sac. Arrows point to masses of fetal syncytium in the outer layers of the sac wall ($\times 150$).

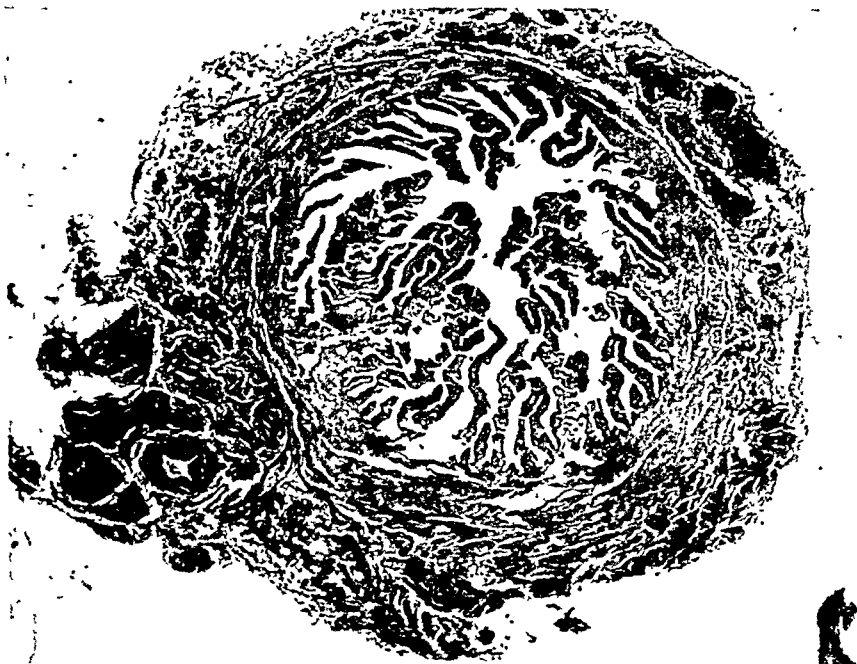


Fig. 6.—Section through distal portion of isthmus of tube. Note the characteristic pleating of the mucosal lining of the distal isthmus of tube. Contrast with similar magnification of interstitial portion of tube shown in Fig. 1. ($\times 35$.)

have penetrated to the very outer surface of the wall. Amnionic membrane can be distinctly discerned as lining the sac. The microscopic sections of the umbilical cord show necrosis and para-umbilical infiltration in the region of the adherent loop and a platelet thrombus occluding the vein at its fetal end.

Accompanying the sac and its contents, there is the distal portion of the Fallopian tube including the fimbria. This portion of tube is normal except for congestion. Microscopically, the structure is characteristic of isthmus and fimbria of a Fallopian tube (Fig. 6).

- Diagnosis:*
1. Macerated full-term interstitial tubal pregnancy
 2. Thrombosis and adherent loop of umbilical cord
 3. Fallopian tube-isthmus and fimbria
 4. Segment of ovary-tuboovarian adhesion.

Summary

1. A case of full-term interstitial pregnancy is presented.
2. The literature reveals a total of 199 cases of interstitial pregnancy reported up to July 1943.
3. Three previous cases of full-term pregnancy have been reported. This report is, therefore, the fourth case of full-term interstitial pregnancy.

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414 STERLING PLACE

LOCAL CHEMOTHERAPY IN THE PROPHYLAXIS OF MASTITIS*

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MUCH experience has been accumulated on the topical application of the sulfonamide compounds since their introduction as prophylactic and curative agents. The experience of the last few years has shown that oral, topical, or oral plus topical medication with sulfonamides will prevent wound infection. There is no doubt now that infection can generally be prevented in minor laceration involving the skin and subcutaneous tissues or superficial muscle layers, without extensive destruction of tissue by the topical application of sulfonamide compounds.

Though a dearth of experimental and clinical reports on sulfonamides has appeared, these are so conflicting that it is difficult to conclude which of the sulfonamides is the "chosen one" for topical use. Long¹ stated, after reviewing these reports: "When all the factors have been considered, it seems reasonable to choose sulfanilamide as the drug of choice for the prophylaxis and treatment of contaminated and infected wounds."

Where sulfanilamide therapy locally has been started, experience has shown that it is necessary to repeat the local application of the drug at each dressing period if both primary and secondary infection is to be prevented. Local therapy with sulfanilamide should be continued until healing is complete.

That sulfanilamide is soluble in tissue fluids and diffuses readily through living tissue and fairly well through dead tissue was demonstrated by Hawking.² He found that it had greater power of concentration and diffusibility; whereas sulfathiazole persisted longer and had higher bacteriostasis, but lower concentration and diffusibility.

Zondek and his associates³ found that sulfanilamide applied percutaneously was absorbed through the skin of rabbits and men, and suggested that this use of sulfanilamide might serve as an auxiliary method of chemotherapeutic treatment in certain cases.

According to Graves,⁴ the combined use of sulfanilamide and sulfathiazole may give better results than either alone; using the sulfanilamide for its ability to go into solution quickly in high concentration and the sulfathiazole because it is more slowly absorbed.

Topical Application of Sulfonamide Compounds

The success of sulfonamide therapy depends on the physical form in which it is applied and the vehicle in which it is dispersed.

*Presented at a meeting of the Pittsburgh Obstetrical and Gynecological Society, April 3, 1944.

In a series of tests to determine the most suitable vehicle for the sulfonamides, Fuller, Hawking and Partridge⁵ found that when sulfanilamide was incorporated into an oily base or an oil in water emulsion, its absorption was much delayed. They also found that incorporation of glycerin or a wetting agent caused little or no influence on the rate of absorption.

Ointments of petrolatum and grease bases are contraindicated according to Kalz and Prinz.⁶ They believe that ointments of this type coat each particle of the sulfonamide with a nonsoluble substance hindering the local action. Pillsbury, et al.⁷ arrived at the same conclusion. "All grease bases (petrolatum, hydrous wool fat or simple ointments) may retain the medicament at the site, but do not allow intimate contact of the agent with the site of infection; they do not mix with the exudate, and are sometimes removed with difficulty and probably allow increased growth of bacteria under the film of grease."

Allantoin—Sulfanilamide—Sulfathiazole Ointment

The base for this ointment was prepared without petrolatum or grease. It was water miscible and contained glycerin, triethanolamine, stearic acid and water.

Allantoin 2 per cent, sulfanilamide 5 per cent and sulfathiazole 5 per cent were incorporated in the above base.⁸ Allantoin, the terminal oxidation product of purine metabolism has been known since 1821. Extracts of comfrey root were used by Macalister⁸ to treat and heal chronic ulcers which failed to respond to other types of treatment. It was determined that the active principle in these extracts was allantoin.

The remarkable success obtained by Baer⁹ with his maggot therapy in chronic suppurative infections was manifested by the characteristics of rapid healing of healthy granulation tissue. Robinson¹⁰ definitely demonstrated that maggot secretions contained allantoin and that the application of allantoin seemed to stimulate a local rather than a generalized granulation. Ratner¹¹ stated that the curative action of surgical maggots in infected lesions was due to allantoin, an excretion of the maggot. On hydrolysis, allantoin yields urea which is responsible for the healing action. Urea has been shown by Olson, et al.¹² to increase the rate of formation of granulation tissue in experimental animals.

Sulfonamide Inhibitors.—It was noticed by some of the earlier workers with the sulfonamides that certain substances inhibited their bacteriostatic action. These sulfonamide inhibitors, it was suggested, were produced by the organisms.

Tsuchiya, et al.,¹³ had demonstrated that the mere presence of urea antagonized the sulfonamide-inhibiting action of at least one of the end products of protein catabolism. Strakosch and Clark¹⁴ found that a mixture of urea and sulfathiazole was more beneficial than sulfathiazole

*Allantoin and Sulfathiazole—made by The National Drug Company, Philadelphia, Pa.

alone; complete epithelialization of lesions was accelerated by from one to five days by the use of sulfathiazole-urea ointment.

The efficacy of allantoin-sulfanilamide ointment in the therapy of surgical infections, was demonstrated by Veal and Klepser.¹⁵ They concluded: "The substitution of allantoin-sulfanilamide ointment for pure sulfanilamide powder allows a prompt resumption of the normal healing process and at the same time maintains a clean wound."

Wallersteiner¹⁶ found that the main compounds that were active in sulfanilamide-fast organisms, were sulfanilamide-urea and to a lesser degree, sulfanilamide-allantoin. These compounds also showed the curious phenomenon of increasing the rate of cell growth and the cell migration of the fibroblasts toward them.

Sensitization.—In recent months reports have been appearing relative to reactions in tissues, and sensitization to sulfonamides by the local application. A comprehensive review of the subject by Cole¹⁷ caused him to issue a warning that sulfonamides should not be administered locally for more than five days because of the danger of sensitizing the individual.

When one considers the enormous volume of sulfonamides which has been produced and consumed as compared to the number of reported drug reactions, it would seem that the sensitization of patients would be more apparent than real.

The purpose of the clinical study undertaken and herein reported was to determine the merits of a combination of allantoin-sulfanilamide-sulfathiazole mixed in a water-miscible base for chemotherapy in the prophylaxis of mastitis.

Procedure.—During the year 1943, each obstetric patient admitted to my service at the Greene County Memorial Hospital, who nursed her infant, the mothers of premature and stillborn being excluded, was treated as follows: within four hours after delivery, the patients' breasts were washed with soap and water, rinsed and blotted dry. The nipples were cleansed with 70 per cent alcohol and dried. The allantoin 2 per cent, sulfanilamide 5 per cent, sulfathiazole 5 per cent ointment was applied with gentle massage to the nipples and areolae, leaving only a thin film on the surface. A sterile piece of gauze was applied to the nipple area and held in place by a supporting cloth binder. An individual tube of the ointment was used for each patient.

Before each nursing period, the mothers' fingers were cleansed with 70 per cent alcohol and the nipple area cleansed with boric acid solution. Following the nursing period, the nipples were again cleansed with boric acid solution, dried and the ointment applied as previously described. A sterile gauze covering and supporting binder were used.

This treatment was continued until the patient was discharged from the hospital, usually on the eighth or tenth day.

Results.—In all, 212 consecutive patients were treated. There were no signs of local or systemic drug reactions observed in mothers or infants. Three patients developed mastitis while in the hospital, and two of these subsequently developed breast abscesses after discharge. These will be discussed in detail later.

Of the 212 patients, 17 or 8 per cent showed a morbidity, i.e., a temperature of 100.4° F. or over on two successive days, excluding the first 24 hours. The cause of morbidity was broken down as follows: Five or 2.3 per cent showed an endometritis; 3 or 1.4 per cent showed a mastitis, as previously mentioned; 3 or 1.4 per cent showed an infection of the episiotomy wound; 2 or 0.9 per cent showed an upper respiratory infection. There was one case of each of the following: Porecaryan section, laparotrachelotomy, pyelitis with an associated nephrolithiasis and post-partum atelectasis.

Of the three patients who developed mastitis, one subsided completely and breast feeding was resumed. The other two seemingly subsided but subsequently developed abscesses after discharge from the hospital. All were primiparas.

The first patient developed a fissure in the left nipple on the fourth post-partum day and on the sixth day, an acute interstitial mastitis in the upper lateral quadrant, was evident. Sulfanilamide-sulfathiazole-allantoin ointment was continued, hot stupes were applied locally, breast feedings were stopped for 48 hours and sulfadiazine was given by mouth. The infection subsided in 36 hours.

The second patient had marked inverted nipples and nursing should probably not have been attempted but a trial was deemed advisable. Acute mastitis developed on the seventh day, subsided under above treatment and nursing was resumed. However, she came back to the hospital on the nineteenth day, when an abscess was incised and drained.

The third patient was delivered of a female infant which had an extensive congenital atelectasis and later a pneumonia of the left upper lobe. This was confirmed by x-ray. The infant lived four days and was out to breast but once. The right breast was used and this one became infected. The ointment was applied but twice to the right breast and once to the left. An acute mastitis developed on the sixth post-partum day and had apparently subsided by the tenth. However, the patient returned on the eighteenth post-partum day when an abscess of the right breast was incised and drained. The pus in both instances looked to be that caused by the staphylococcus.

Discussion

The first patient developed a mastitis secondary to a small fissure. She responded well to local and general treatment.

In the second patient who possessed such marked inverted nipples, the ointment obviously was not effective. Nursing was instituted and continued here with the full knowledge of what might result. A genuine trial of the ointment was deemed advisable and warranted.

In the third patient, the sick infant should not have been put to breast, not only for its own sake, but because of the possibility of introducing infection into the nipple. The ointment should have been used continuously for at least five days.

Conclusions

1. The local application of allantoin 2 per cent, sulfanilamide 5 per cent, sulfathiazole 5 per cent in a water-miscible base is a safe pro-

cedure, and in this number of cases caused no local or systemic reaction to mother or baby.

2. Sensitization of the patient is a possibility as reported by Cole, but the small amount of drug undoubtedly absorbed systemically makes this seem remote.

3. Markedly inverted or potentially infected nipples should be treated with the ointment but nursing should be prohibited.

4. While it cannot positively be asserted, it is felt that the use of this allantoin—sulfanilamide—sulfathiazole ointment, as described herein, helps to prevent mastitis. Certainly its use is more rational than the ointments used heretofore.

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CHOREA GRAVIDARUM: WITH THE REPORT OF A CASE

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TO OBSERVE a patient with chorea gravidarum is an unique and unforgettable experience. It is unique in that cases are seldom seen more than once in the entire practice of any obstetrician, if at all. The reported incidence is widely divergent. Berg² states that, at the St. Louis City Hospital, only 2 cases in 12,000 deliveries were recorded during the course of fifteen years. At the John Gaston Hospital, Memphis, a teaching institution, no case has been recorded in over 28,000 deliveries covering a period of twenty-eight years. Willson and Preece,¹² however, estimate the incidence as 1 in 2,500 deliveries. It is an unforgettable experience in that the clinical picture which it presents is perhaps the most distressing of all the complications of pregnancy. Further, although a well-recognized entity early in the nineteenth century, the condition still compels interest because of its much disputed origin, the variability of its manifestations and the number of views as to their interpretation, as well as the problem of its management.

Concerning the origin of chorea gravidarum, opinion is largely divided between the theory that it is a Sydenham's chorea appearing in pregnancy and is therefore of an infectious nature, and the theory that it is due to toxemia. An infectious etiology is apparently established in a number of cases by a history of rheumatic fever or scarlet fever in childhood, and frequently an early chorea. In this group, arthritis and endocarditis or other cardiac disease is often associated. An early onset and the fact that the chorea may recur with successive pregnancies is likewise in favor of this origin. On the other hand, many cases are reported in which there is no history of infection or earlier chorea, and no evidence of a heart lesion; in these, the symptoms are believed by many observers to be a manifestation of toxemia. A toxic origin is also suggested by an absence of fever, a prompt subsidence of symptoms after termination of the pregnancy, and frequently other signs of toxemia.

Unquestionably, there is also a strong element of neurosis in chorea gravidarum. This element is probably primarily constitutional, and is aggravated by emotional disturbances pertinent to the pregnant state. Whitmore¹¹ believes that fatigue due to increased emotionalism is a significant factor in young primipara. Early environment may also have some influence. Weigner¹⁰ reports that Gerty and his associates, in a seven-year study of 150 children with chorea, together with a control group who had rheumatic fever but no chorea, found that those with chorea came from families wherein there was a great deal of emotional turmoil and social maladjustment. This history was not given by those who had rheumatic fever without chorea. Weigner also quotes Sahli as

having pointed out that movements of the fetus are choreiform in nature; that muscle movements become orderly and purposeful after birth; and that perhaps this constitutional tendency is an expression of failure of normal development. One may thus explain the cases of chorea wherein only certain muscle groups are affected. It is Weigner's opinion, therefore, that chorea gravidarum should be regarded as an expression of a defective constitutional "anlage," which may be precipitated by various factors, as infection, toxicity or nervous influences originating from acute emotional trauma and psychic conflict relating to pregnancy. The likelihood of a neurotic or psychic factor is supported by many reports of cases in which the attack has been preceded by worry or immediately induced by some shocking or frightening incident.

Pathologically, chorea gravidarum is a low-grade encephalitis. Several investigators have reported finding congestion and hemorrhage in almost every part of the cerebrum in autopsy studies. The movements are conceded to have their stimulus, however, in the basal ganglia, wherein the process is most severe and may be both degenerative and inflammatory in character. Brian and Gerundo³ reported a case in which, in addition to the brain, the liver, kidneys and spleen presented degenerative and inflammatory changes. There were no signs of past or present endocarditis. From these findings, which bear a close resemblance to those encountered in fatal eclampsias, they believe their case was toxic in origin. The onset of the symptoms during the sixth month of pregnancy and the clinical course bore out this opinion. They conclude that a distinction between the toxemic and rheumatic types may be made by the clinical course and nephrohepatic lesions.

Chorea gravidarum appears to have a predilection for young women, the average age being between twenty and twenty-five years. Rarely is it seen in patients beyond thirty years of age. As Berg² has pointed out, it is perhaps partly because of this age incidence that primipara are more often affected. It may, however, appear for the first time in multipara. The patient observed by Brian and Gerundo³ first had chorea during her second pregnancy, at the age of thirty-five. Not infrequently, moreover, the movements appear in more than one pregnancy. Scheftel's⁹ patient had chorea with three successive pregnancies, and French and Hicks⁷ describe a case in which chorea complicated the first pregnancy, was absent in the three succeeding ones, and recurred during the fifth.

Both the maternal and fetal mortality are variously quoted. In a study of 951 choreic pregnancies in 797 patients, Willson and Preece¹² found the maternal death rate to be 13.1 per cent for those delivered spontaneously at term, whereas it was 33.3 per cent for those terminated artificially. These were the more severe cases; of the patients with the mild forms who were delivered spontaneously at term, the rate was only 1.9 per cent. The fetal mortality is generally reported as approximately twice that of the mother. DeLee⁷ estimated the maternal mortality

as 20 to 30 per cent, and the fetal mortality as over 50 per cent. According to Royston,⁶ pregnancy in a choreic individual is not necessarily serious, whereas a chorea appearing for the first time only after conception is always of grave import, and failure to differentiate these two conditions probably explains the marked variation in mortality figures.

With few exceptions, infants delivered at term are normal. DeLee⁷ states that an occasional infant is born with chorea. In reported cases, abnormalities, when present, were confined to the head and spine. Two of the infants in Willson and Preece's¹² series were born with spina bifida and hydrocephalus, and a third had hydrocephalus alone. Campbell⁴ reported a case in which the patient gave birth to a baby with a marked microthalamus and facial asymmetry. Scheftel's⁹ patient was delivered of an infant with the Klippel-Feil syndrome at her third pregnancy complicated by chorea.

The symptoms of chorea usually have their incipieney during the early months of gestation, though in a number of cases they do not appear until the second or third trimester, and in a few not until after delivery. They are generally mild in the beginning, consisting merely of an intermittent coarse twitching or numbness of a few muscle groups, such as those of one hand and arm, or one upper and lower extremity of the same side. The left side is most often affected. In the majority of cases, the movements remain mild in character and cease with sleep. In others, they increase in severity and extent; with the approach of the puerperium practically all the muscles of the body may be continuously and violently contracted, necessitating forceful restraint of the patient in bed. The muscles of the face and neck are usually involved, causing impairment or total loss of the power of speech and deglutition. In such cases, the prognosis is grave indeed. The patient is not only soon exhausted from the constant movement and loss of sleep, but suffers from malnutrition incident to the difficulty in feeding.

Personality changes are commonly associated with the choreic symptoms, occasionally preceding them by weeks or months. At first, these changes may consist only of an irritability, or a depression or melancholia, and often are associated with a more or less severe headache. As the movements increase, the psychic symptoms also increase until, in the later stages of the disease, the patient may have hallucinations, or may even exhibit a complete mental incapacity.

The temperature and pulse rate may or may not be elevated throughout the course of the illness. When present in the more severe forms, and especially when associated with pronounced psychic manifestations, fever adds materially to the gravity of the prognosis.

The diagnosis of chorea gravidarum is usually obvious almost at a glance. In the early stages of pregnancy, one may need to make a differentiation from hysteria or a pure neurosis. The differentiation from hysteria should not be difficult by the rhythmical movements of the latter, in contrast to the incoordinated and irregular movements of

chorea. Since a strong neurotic element is often present in chorea, a neurosis may be less easily distinguished. Flamma⁶ reported a case of supposed chorea in which he feigned an interruption of pregnancy and the patient promptly recovered. Such cases, however, are rare.

The clinical course is not unlike that of Sydenham's chorea. A large proportion of patients recover before term, especially those with a mild form of the disease. If the patient comes to term, the movements increase during labor, but usually begin to subside almost immediately after delivery and disappear completely within a few weeks. In some cases, however, recovery is slow, requiring months.

When feasible, conservative treatment may bring about a quiescence of the movements. Mild cases are often amenable to quiet and rest, wholesome food, and the use of bromides and barbiturates. Several authors have reported a definite response to one or more small transfusions of blood from a healthy pregnant woman, as suggested by Albrecht.¹ This treatment is probably efficacious in those cases wherein toxemia plays a prominent role.

In severe cases, termination of the pregnancy is advisable. The sooner this is done, the better, as the mortality is exceedingly high when operation is delayed. The presence of fever is an added indication for intervention. Abortion is regarded as the procedure of choice, though cesarean section is usually preferable if the pregnancy is well advanced, or the choreic movements become violent.

Case Report

Mrs. T. C. D., aged 20 years, was first observed during the fourth month of her first pregnancy. Her family history was irrelative insofar as mental or physical disease was concerned. Her mother had died of tuberculosis and her father had been killed in an accident while she was still a child, and she had been reared by an aunt. Aside from these tragedies, her childhood had not been unhappy. She had had whooping cough and measles, but gave no history of rheumatic fever, scarlet fever or chorea. Her menstrual history was normal. She had been married to a medical student for almost two years, and stated that she was happy in her marriage. The only other finding which threw any light upon the condition was the fact that she had been working rather strenuously in a nursery school for more than a year, and was considerably fatigued as a consequence.

Her symptoms had begun two months previously, with an intermittent numbness in her left hand, arm and shoulder. At the time of her first visit, she was experiencing little inconvenience other than some difficulty in combing her hair and picking up objects. Believing this might be due to malnutrition, she was given vitamin B₁. Within a short while, however, the left lower extremity became affected and the symptoms increased in severity, until both the upper and lower left extremities were involved in clonic and sometimes tetanic contractions. At the same time, choreic movements appeared in her forehead and left upper lip. The spasmodic contractions were now more frequent, and were aggravated by mental or muscular effort.

Coincident with these physical manifestations, it was observed that the patient was exceedingly nervous and easily upset, and that her entire personality was undergoing a change. Normally of a cheerful disposition, she became depressed and manifested a desire to be alone and in the dark. She complained, also, of a crescendo type of temporal headache, sometimes unilateral and sometimes bilateral. She slept poorly, had little appetite, and appeared emaciated. Her weight had not changed, however, probably because of the fetus. At times she had a temperature of 99.5° F. to 100.5° F., and a pulse rate of 96 to 100. She had not experienced any dizziness, vertigo nor tinnitus, nor had she had any nausea, emesis or other gastrointestinal disturbances during pregnancy.

The patient was at this time examined by a psychiatrist, though nothing was found to account for her symptoms. A physical examination by an internist failed to reveal any foci of infection, and aside from an increase in heart rate, there was no cardiac abnormality. The sedimentation rate was elevated, but not to a degree which would indicate a previous rheumatic fever.

Despite practically constant rest in bed, a high vitamin diet, and sedation to promote sleep, the symptoms continued and gradually increased until, during the sixth month of pregnancy, they suddenly became quite severe. On returning home one afternoon, her husband found her alternately sitting up and lying down in bed, crying, and in a state of constant and violent motion. The psychiatrist who had examined her previously was called, and recommended termination of the pregnancy. The patient was brought to our office the following day. She was still crying, her facial muscles were twitching, and it was obvious that all the choreic movements had become materially worse since her last observation. Physical examination disclosed increased reflexes over the left half of the body, and choreiform movements of the left arm and shoulder and left leg, with a bilateral involvement of the eyes, tongue and masseter muscles. There was also a beginning chorea of the right half of the body. Sensation appeared normal. Her pulse rate was 72, blood pressure 103/56, and temperature normal. In view of the obvious spread and increased violence of the contractions, together with the progressive mental changes, interruption of the pregnancy was considered advisable. Since the patient was in the sixth month of gestation, a cesarean section was performed.

On awakening from the anesthetic, the patient stated that she felt normal and sane again, and that the previous month was practically a blank in her memory. During the three days immediately following operation, the contractions were exaggerated, but thereafter began to subside and had practically disappeared by the time she left the hospital, at the end of two weeks. So far as the chorea is concerned, she has had no further trouble. A few weeks after operation, however, she developed generalized joint pains, necessitating treatment by heat and massage.

Comment

This patient presented the typical clinical picture of chorea gravidarum. The case is unusual in that we were unable to determine definitely the cause. The appearance of the symptoms during the first trimester of pregnancy, and the lack of organic disturbances seemed to rule out toxemia as the etiologic factor. We are convinced that

fatigue was a strong influence and, despite the clinical history and the absence of a heart lesion, are inclined to believe that either the attack of measles, or an unsuspected mild rheumatic fever in childhood was primarily responsible. The early onset, the intermittent low-grade fever, and the attack of acute arthritis after recovery from the operation support this view.

Summary

1. Chorea gravidarum is a rare disease which affects chiefly young primipara. It is also observed in multipara, however, and occasionally recurs with successive pregnancies.

2. Pathologically, it is a low-grade encephalitis, apparently being precipitated by the toxemia of pregnancy, or originating in an earlier infectious disease, such as rheumatic or scarlet fever. A defective constitutional *anlage* is suggested as a fundamental requisite, and other influences, including fatigue, heredity and environment, are often significant.

3. The disease is distinguished chiefly by choreiform movements and mental changes.

4. The majority of cases are of mild degree and subside under conservative treatment. Others become severe, necessitating termination of the pregnancy. The origin of the symptoms is obscure, though it is believed that a previous infection was the underlying factor.

5. A case of progressive chorea gravidarum is presented, in which cesarean section was performed during the sixth month of gestation.

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VOLVULUS COMPLICATING PREGNANCY*

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THE first report of volvulus complicating pregnancy appeared in the literature in 1885. At that time, Braun, in Germany, reported a case of volvulus of the sigmoid colon complicating pregnancy at term. His patient died and the diagnosis was made at autopsy. Since that time there have appeared seventy-six reports of this condition. We wish to add two cases to this series, both occurring in the same patient and in succeeding pregnancies, the first in 1941, and the second in 1943. We have also attempted to collect all reported cases since 1931 when they were last summarized by André Charles Lambert. From time to time several investigators have, to an extent, collected the cases on record. König in 1922 and Radaeli in 1928 presented partial summaries. The most complete collection was presented in 1931 by Lambert of Paris in his Doctor's Thesis. We have been able to find only three cases that he missed: (1) Cattell, 1891; (2) Green, 1912; (3) White, 1914.

Lambert's excellent and very complete report in 1931 consisted of sixty-one cases and we have found thirteen since then plus the three he failed to include. Of these sixty-one, he found that twenty-nine cases occurred in the sigmoid, sixteen in other parts of the large intestine, and sixteen in the small intestine.

The eighteen cases which we will add are localized as follows: twelve in the sigmoid, three in the large intestine other than sigmoid, and three in the small intestine. It is most surprising that of the total number of cases only four have been reported in the United States: (1) Cattell, 1891; (2) Flower, 1912; (3) Green, 1912; (4) Kornfeld and Daichman, 1934. Our cases therefore become the fifth and sixth reported in this country.

Report of Cases

This patient, H. J., was an eighteen-year-old colored female, a primigravida, who was first seen in the obstetrical outpatient clinic of the University of Maryland School of Medicine on April 23, 1941. She was found to be fourteen to sixteen weeks pregnant, and her estimated date of confinement was October, 1941. She was given antiluetic therapy and her ante-partum course was normal until August 1, 1941. At that time, when the patient was twenty-four weeks pregnant, she developed nausea, vomiting and abdominal pains. She was seen in the accident room on August 6, 1941, with the above complaints, and was treated unsuccessfully with enemas. She was sent home and was seen again the

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following day at which time castor oil and another enema were prescribed with no results. On August 8, 1941, the patient returned to the accident room with signs of partial intestinal obstruction and was admitted to the obstetric service. She was treated with intravenous fluids, enemas, and a rectal tube without relief. The blood chemistry and blood picture were normal except for a hemoglobin of 50 per cent.

The patient did not improve and on August 9, 1941, an exploratory laparotomy was done, under spinal anesthesia, through a low left paramedian incision. An obstructing lesion was demonstrated in the pelvis that was described as "giving the sensation of a twisted towel." When the dilated descending colon was delivered through the wound, the condition was found to be a volvulus twisted two and one-half times in a counterclockwise direction. When this was reduced, a large amount of gas was expelled through the previously inserted rectal tube and the markedly distended colon collapsed. The wound was then closed in the routine manner and the patient withstood the procedure fairly well. She received large doses of corpus luteum substance for the first postoperative week, and was discharged to the prenatal clinic on August 24, 1941, in good condition.

The patient went into labor spontaneously on October 19, 1941, some two months later, and was delivered of a full-term living child, weighing 5 pounds 8 ounces by breech extraction. The post-partum course was entirely normal.

There is no further record until January 6, 1943, when she presented herself at the prenatal clinic, and was found to be again pregnant, duration twelve weeks.

The second prenatal course was uneventful until April 11, 1943. At that time, when she was twenty-eight weeks pregnant, she was seen in the accident room, her complaint being abdominal pain and severe constipation of five days' duration. Examination revealed the uterus to be well above the umbilicus and freely movable. The upper abdomen was distended but not tight, and readily showed the pattern of a markedly dilated transverse colon. Enemas were ineffectual. A flat film of the abdomen revealed no pathologic condition other than the markedly distended colon. The patient told us that she had been operated upon in 1941 for "locked bowels," and after her old chart was consulted the diagnosis was readily made.

The operation was under spinal anesthesia through the previous left paramedian scar. Again the sigmoid was found to be twisted two times in a counterclockwise direction. The mesentery of the descending and sigmoid colon was markedly lengthened and the gut was four to five times its normal caliber. The colon was delivered and untwisted two complete turns. The gas was expelled through the previously inserted rectal tube, the colon collapsed, and the abdomen was closed. The patient was given large doses of corpus luteum substance both before and for several days after this operation. The postoperative course was uneventful, and she was discharged to the prenatal clinic on April 28, 1943.

She remained symptom free until May 16, 1943, when she again returned to the hospital complaining of abdominal pains, distention, nausea, and severe constipation of forty-eight hours' duration. Examination revealed a pregnancy of thirty-six weeks and the same findings as before, and repeated efforts to reduce the volvulus with enemas with

the patient in shock position were unsuccessful. At this time the question of interrupting the pregnancy instead of operation was considered but was discarded.

Large doses of corpus luteum substance were given pre- and post-operative, and the operation was again through the old left lower scar and under spinal anesthesia. The descending and sigmoid colon were posterior to the enlarged uterus and they were delivered after considerable difficulty. The sigmoid was twisted one and one-half times in a counterclockwise direction and was reduced and decompressed as previously. However, the colon and its mesentery were markedly edematous and the tissues were in much worse condition than at the previous operation.

The following morning the patient went into labor and her membranes ruptured at 2:30 P.M. At 3:25 P.M. she was delivered under gas-oxygen anesthesia, of a thirty-six-week living male child, weight 4 pounds 11 ounces by breech extraction.

The postoperative and postpartum courses were uneventful and the patient was discharged in good condition on June 10, 1943. The child was kept in the premature nursery.

It was planned, at the time of discharge to bring the patient back after the uterus had become involuted and the tissues of the intestinal tract had returned to normal; give her a course of sulfasuxidine, and then resect the redundant colon and do a primary anastomosis. However, this was not to follow, because on June 21, 1943, five weeks following delivery, and eleven days following discharge, the patient again presented herself at the hospital complaining of colicky abdominal pains and of severe constipation for thirty-six hours. Again the abdomen was distended and the pattern of the colon was readily seen on the abdominal wall. Enemas being ineffectual, the abdomen was opened for the fourth time at the same site. On this occasion, the volvulus was at a higher level in the sigmoid and was rotated one and one-half times in a clockwise direction. In other words, the colon was rotated in the opposite direction from the three previous times. Following Pomeroy sterilization, a Mickulicz procedure was done and about forty-five to fifty centimeters of the redundant sigmoid and descending colon were resected. The clamp was removed on the fourth postoperative day and the colostomy functioned satisfactorily. The spur was crushed while the patient was making her usual uneventful recovery. The patient was discharged on July 23, 1943, with the colostomy still functioning, but she was also passing fecal material *per rectum*.

The colostomy did not close spontaneously and the patient was readmitted September 1, 1943. The spur was crushed more deeply and on September 13, 1943, the colostomy was closed. The wound developed a slight subcutaneous infection but the patient was discharged in good condition September 30, 1943. At the present time both mother and baby are in good health.

Discussion

A statistical study of the cases we have collected shows that age apparently exerts no influence on the disease. The cases range from eighteen to forty-one years. Under twenty years—two cases; twenty-one to thirty years—seven cases; thirty-one to forty-one years—six

cases. Three reports did not state the patients' ages. The greater number of cases under thirty years, of course, is due to the age group of pregnancy.

Three of the patients were primigravidas, twelve were multigravidas, and three authors did not report the parity. Thus it would appear that multiparity of itself predisposes to volvulus, possibly because of relaxation of the abdominal wall musculature.

At what stage of pregnancy is volvulus most frequent? Lambert states that he found the greatest number at term or during labor. We have found our cases distributed as follows: first trimester—one case; second trimester—four cases; third trimester—ten cases; post partum—four cases. This totals nineteen, because in her second pregnancy our patient had both ante-partum and post-partum volvulus. It is rather interesting that the greatest incidence should be at a time when the abdomen is so distended by the pregnant uterus that torsion of abdominal contents would seem most difficult. On the other hand, Spence states that, "In view of the rapid change of position of the intestine after delivery of a full-term child, it is surprising perhaps that volvulus does not happen more frequently immediately post partum."

The etiology of volvulus in pregnancy is not well known, a demonstrable cause being present only occasionally. Cattell's case followed an old ectopic pregnancy which had become attached to the small intestine and thus torsion was initiated. There are occasional cases of improper rotation of the gut in the course of development and the enlargement of the uterus is sufficient to start the torsion as reported by Donald. In the pelvic cases there is almost always an abnormally long mesocolon, without which torsion cannot take place. Some patients give a history of trauma or strain; however, as a cause, this probably should be discounted. One patient reported by Lambert had a previous history of salpingitis and several patients gave histories of persistent constipation over a period of days, weeks, or years.

The degree of torsion varied from 135 to 800 degrees. While torsion may be in either direction, there seems to be a greater incidence counterclockwise. The condition of the intestines may be any state between slight engorgement and gangrene, depending upon the duration of the volvulus and the amount of strangulation. Peritoneal bands have been responsible for instituting torsion in a few cases.

The symptoms of volvulus complicating pregnancy, like uncomplicated volvulus, are those of intestinal obstruction. Usually the patient gives a history of varying degrees of constipation for several days. This is followed by abdominal pain which is colicky in nature and becomes progressively severe. Vomiting is a variable symptom, depending upon the location of the volvulus. When it is in the small intestine, vomiting is early and protracted; while in the large intestine volvulus, vomiting is not a prominent symptom and usually develops late. Enemas are usu-

ally ineffectual in the colonic type while they are effectual in the small intestinal variety. This fact is often misleading in diagnosis. Examination of the abdomen usually will reveal a marked distention of the intestine above the volvulus. Abdominal tenderness is not a consistent finding, and when present, is usually generalized. Temperature and pulse depend upon the patient's general state of hydration, toxicity, and peritoneal irritation. The post-partum cases are particularly perplexing in the presence of post-partum infection where the classical signs of obstruction are frequently present, but they subside under treatment for the infection and purgation. The signs are most clear when the pregnancy is early. Fluid in the peritoneal cavity is rarely demonstrated although it is usually present.

The diagnosis of intestinal obstruction is usually fairly simple, but to state that it is due to volvulus is a very different matter. This is especially true in the presence of a well-advanced pregnancy. Masses other than the uterus are difficult to palpate. This is not particularly essential, however, for the important thing is to make the diagnosis of obstruction, and to take proper steps to relieve it. Review of the cases reported reveals few instances in which the diagnosis of volvulus was made before operation or autopsy.

The prognosis is to be viewed from two points: that of the mother and that of the child. We have but three cases involving the small intestines and hesitate to draw conclusions in this group. In the large intestine group, however, there are fifteen cases. Here the maternal mortality was 26.33 per cent (4 deaths). (1) Green, 1912, sudden death due to peripheral vascular collapse twelve hours postoperative; (2) White, 1914, patient died of peritonitis six days following resection of gangrenous cecum and ascending colon; (3) Kornfeld and Daichman, 1934, patient died about two weeks postoperative of peritonitis, following resection of gangrenous sigmoid; (4) Rose, 1941, patient died post partum, unoperated, diagnosis at autopsy. The fetal mortality in this group was the same as the maternal, 26.33 per cent. This includes one patient who died undelivered.

If, however, we examine only cases operated upon early where resection was not necessary there is only one death, Green's patient who died of shock. In this group one child was born dead and one was undelivered.

Thus it appears that the time of operation bears a great influence on the prognosis for both mother and child. There were fifteen laparotomies with three deaths, 20 per cent mortality. Three patients were not operated upon and all died, 100 per cent mortality.

There is only one treatment for this condition, namely, surgical. The obstruction must be relieved and reduction is the only way to accomplish relief of the obstruction. It would seem that the best results are obtained when the volvulus can be merely reduced and the pregnancy not

disturbed. This is true regardless of the duration of the pregnancy. Our patient was treated in this way and we delivered a living child at each pregnancy. Fear of rupture of the abdominal wound, if labor intervenes shortly after operation, probably has little foundation. The administration of large amounts of corpus luteum substance both before and after operation may prevent the onset of labor. This treatment and therapy apparently permitted our patient to continue her pregnancies on both occasions. The first pregnancy was carried to term. During the second pregnancy, labor was again prevented following the first operation at twenty-eight weeks. The therapy failed, however, the second time at thirty-six weeks.

Summary and Conclusions

1. Presentation of eighteen cases of volvulus complicating pregnancy (not previously reported) including two original cases.
2. Total cases reported are localized as follows: small intestine—19 cases; large intestine other than sigmoid—19 cases; sigmoid—41 cases.
3. Presentation of a patient who has been operated upon four times for volvulus of the pelvic colon associated with two pregnancies.
4. The patient did not go into labor following the early operations (during her sixth month in 1941, and during the seventh month in 1943). Large doses of corpus luteum substance were given before and after operation. However, labor followed the operation at the thirty-sixth week of gestation despite the same medication.
5. Volvulus occurring with pregnancy is a very interesting and a very rare complication. There have been only six cases reported in the United States and seventy-three cases reported abroad.
6. The etiology of this complication is not clear and the only relatively consistent pathologic finding is in elongated mesocolon in those cases involving the sigmoid colon.
7. The diagnosis of volvulus is very difficult but intestinal obstruction is usually quite apparent.
8. The symptoms are those of obstruction depending upon the location of the blockage.
9. The prognosis for mother and child is good if early diagnosis and treatment are available. Otherwise, the prognosis is poor for both.
10. The treatment is surgical relief of the obstructing volvulus. Termination of pregnancy does not appear to be indicated.
11. It would seem that large doses of corpus luteum substance pre- and postoperatively are of considerable help in allaying the sensitivity of the uterus in the first and second trimesters, when laparotomy is done, but of doubtful value in the third trimester. This has been our experience in several other instances when abdominal operations were necessary during pregnancy.

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PREGNANCY AND DIABETES

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DIABETES as a complication of pregnancy is encountered somewhat infrequently; however, during the past decade about sixty articles have appeared in the American and British literature on the subject. This alone denotes roughly the importance attached to pregnant diabetic patients by both the obstetrician and the internist.

The purpose of this communication is to present an analysis of the diabetics who have undergone confinement at the University Hospitals of Cleveland during the past eleven years, and to review briefly certain important features relative to the subject in the recent literature.

Forty-four diabetic pregnancies have been delivered in this hospital during the period from January, 1933, through March, 1944. Four cases in which the diagnosis of diabetes was questionable from information obtained from the records were not included in this series.

The age distribution was roughly that of a normal group of parturients. The youngest patient was 17 years of age and the oldest was 43. Thirteen of the group were primigravidas.

It is a well-recognized fact that the occurrence of stillbirths in diabetics is high. The time of fetal death is frequently after the thirty-sixth week of gestation. Kramer¹ found that 60 (25 per cent) of 238 cases collected from the literature resulted in stillborn infants. In our series there were seven (16 per cent) stillbirths. There were five neonatal deaths. Translating these figures into terms of living infants discharged from the hospital, usually between the tenth and fourteenth days of life, the survival incidence was 73 per cent. Ten of the multiparas had had a total of eleven previous stillbirths.

Nine infants (20 per cent) in this group of cases weighed over 4,000 grams. Speculations as to the cause of the increase in infant weight in diabetic mothers has been thoroughly discussed in much of the literature. Maternal hyperglycemia was the favorite explanation of the occurrence of the so-called "giant" infants of diabetics until the work of Snyder² and Hoopes.³ Overdeveloped offspring in animals were produced by these investigators by the injection of prolan. This work and that of others⁴ suggests that the correct explanation is on the basis of hormonal derangement. It is of interest to note five of the nine infants of excessive size in this series were from mothers whose hyperglycemia was mild to the degree that it could be controlled by diet alone.

Congenital anomalies are said to be found more frequently in infants born of diabetic patients. In this group there was only one infant which demonstrated a congenital defect; this infant dying from congenital heart disease in the third day of life. White⁵ reports seven (4.2 per cent) abnormalities in a group of 166 babies from diabetic patients.

The most common complication encountered in pregnant diabetics is pre-eclampsia. In a study of 43 pregnancies in 38 diabetics, Allen⁶

found that 70 per cent showed one or more signs of toxemia. He made the interesting observation that with the exception of two patients, all of the toxemias weighed between 160 and 240 pounds. Toxemia and eclampsia occur nearly fifty times more frequently in diabetics according to White.⁷ Fifty per cent of the cases studied by Potter and Adair⁸ were toxemias. Mengert and Laughlin⁹ found that 24 per cent of their cases were pre-eclamptics. In our series there were twelve cases of pre-eclamptic toxemia, an incidence of 27 per cent. No cases of eclampsia occurred. Three of the seven stillborn infants were from pre-eclamptic patients.

Hydramnios is mentioned in the literature as one of the complications of diabetic pregnancies. It has been suggested that better control of the diabetes may account for a decrease in the number of cases of hydramnios.⁵ We have had one case of hydramnios in our group of patients.

There were no cases of diabetic coma during labor or during the puerperium; however, two cases of hypoglycemia due to excessive dosage of insulin did occur. Both of these occurred during the puerperium.

It is generally believed that puerperal sepsis is rare in the diabetic. This is borne out in this series in that only three patients delivered per vaginam, demonstrated a post-partum morbidity (10 per cent of the vaginal deliveries) and in none of these was the morbidity severe. The morbidity incidence in the cases delivered by section was 43 per cent which is not considered high for this type of operation. There were no wound complications of significance.

There were two cases of maternal mortality. Both of these patients died of pneumonitis following aspiration of vomitus at the time of section. In neither of these sections was diabetes the indication for operation.

Stander and Peckham¹⁰ and others have pointed out that some diabetics improve during the latter part of their pregnancies. It is believed by some that this is due to an increased supply of insulin from the fetus. Excess utilization of maternal carbohydrates has also been considered. Although this change for the better does take place in some cases, it is probably not the rule. Reuter¹¹ states that about 10 per cent improve, 40 per cent show no change and 50 per cent become worse. As regards the status of the infant pancreas in maternal carbohydrate metabolism, the recent work of Helwig¹² is noteworthy. In a study of eighteen fetal pancreases, nine of which were from children born of diabetic mothers, it was concluded that although in general there was an hypertrophy and hyperplasia of the insular tissue in the infants of the diabetic group, this finding was not constant, nor was there a correlation between the amount of insular tissue and the blood sugar level of the infant. Potter, Seckel and Stryker¹³ are of this same opinion.

During the early months of pregnancy abortion occurs frequently. This is particularly true in cases of uncontrolled diabetes in which cases abortions are said to be six times more frequent than in the controlled patients.⁷ Ronsheim¹⁷ estimates that 50 per cent of diabetic pregnancies end in abortion or premature birth. Acidosis, poorly understood changes in the reproductive system,¹⁸ failure of the normal glycogen deposition in the diabetic endometrium⁷ are the most favored attempts to explain these early mishaps in diabetic pregnancies.

Any report on diabetes associated with pregnancy would be incomplete should mention of the work of Smith and Smith⁴ be omitted. These investigators found an imbalance between prolactin and estrin levels

in pre-eclampsia. They also observed a close relationship between this abnormal hormone picture and late accidents of the pregnant diabetic, i.e., toxemia and stillbirths. Similar studies on pre-eclamptic patients have been made by Taylor and Seadron.¹⁴ Their observations, however, failed to substantiate the Smiths' conclusions.

White, Titus, Joslin and Hunt,¹⁵ basing a therapeutic approach to the problem on the work of Smith and Smith, have instituted substitutional therapy with massive dosage of estrogenic hormone and progestin. In their hands this has given remarkable results in controlling pre-eclampsia, stillbirths and excessively large babies. Stilbestrol in doses of 40 to 120 milligrams has been used in place of the natural estrogens with equally spectacular results.¹⁶

Methods of delivery of the diabetic vary greatly.^{9, 19-21} We are of the opinion that individualization of cases is of greatest importance, and because of this belief, the methods employed in this clinic can be classified as a group as being neither conservative nor radical. Delivery by vaginal route was effected in 68 per cent of the cases presented, however, no hesitancy is felt in selecting section as the method of choice in certain cases. Fourteen (32 per cent) of our cases were delivered by cesarean section. Four of the sections, however, were done because of conditions other than diabetes. These indications were placenta previa, premature separation of the placenta, failure of the fetal head to enter the pelvis following thirty-one hours of labor, and a previous section.

Induction of labor is done infrequently in this clinic except on rather strict medical or obstetrical indications. It is believed that the infant of a diabetic mother will not tolerate a prolonged labor as well as the infant of a normal patient. Since the labors following induction are not infrequently prolonged, we are of the opinion that this method of bringing about premature labor to avert intrauterine death which may take place close to term is of use in a very selected number of cases. In four of our cases labor was induced. These four cases were multiparas and three were delivered of living babies. In the fourth case, the fetus was dead prior to induction of labor.

We are in agreement with R. S. Titus²² in that the child is of such importance to some of these diabetic mothers that cesarean section cannot be considered a radical procedure for terminating their pregnancies prematurely and increasing their chances of having a living baby. The indications for cesarean section in diabetic patients may be listed as follows: (1) Purely obstetrical, e.g., cephalopelvic disproportion, placenta previa, etc.; (2) patients with viable babies in whom there are progressive elevations of blood pressure or other signs of increasing pre-eclampsia; (3) certain cases in which there have been previous stillbirths which were attributed to diabetes; (4) elderly primigravidas; (5) any case in which the delivery of a living infant is of great importance to the patient; and (6) the occasional case in which the diabetes becomes uncontrollable with the advancement of pregnancy and the baby is viable.

In cases in which section is done on fetal indications, the time for operation should be about three weeks before the expected date of confinement. Most infants of diabetics will be found to be mature at this age. X-rays may be of value in determining the size of the fetus, this being used as a guide to the time for delivery. This procedure must be correlated with the menstrual history of the patient and clinical judgment and not solely relied upon as an index of viability.

When an artificial termination of pregnancy, section or induction, is decided upon, it must be kept in mind that the size of the fetus of a diabetic is not an infallible criterion to the maturity of the infant. Titus²³ cites two cases in which the infants of diabetic patients, delivered by section, died of prematurity. These infants weighed 3,456 grams and 3,870 grams.

We wish to emphasize that performing a section simply because a tubal sterilization is to be done is not a sound obstetric procedure. A sterilizing operation can be done in the early puerperium with a negligible risk to the patient, and if it is done at this time, it is an extremely simple operation.

Summary and Conclusions

Forty-four diabetic pregnancies delivered in the University Hospitals of Cleveland during the past eleven years are presented. Our statistics are in general agreement with most of those of others in the recent literature as regards fetal and maternal complications.

Whereas we do not sanction delivery by cesarean section in every diabetic pregnancy, we consider this method of delivery preferable in many cases. The indications for cesarean section in diabetic pregnancies are outlined.

Careful study and individualization of cases offer the best hope for assuring pregnant diabetics of successful terminations of their gestations.

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THECA-CELL TUMORS OF THE OVARY

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ALTHOUGH fibromatous ovarian tumors associated with menstrual irregularities or postmenopausal bleeding had been reported previously in the scientific literature, it was not until 1932 when Loeffler and Priesel¹ presented six cases of "fibroma theca cellulare xanthomatodes ovarii" that gynecologists and pathologists recognized a new clinical entity. This report sent many gynecologic pathologists scurrying to their laboratory files, with the result that a number of ovarian tumors previously diagnosed as fibromas were reclassified as theca-cell tumors.

To date, a total of approximately 82¹⁻³⁹ such tumors have been reported in the world literature. There have also been a number of other tumors reported which, though not classified as theca-cell tumors, would seemingly fall into this group from the data presented.⁴⁰⁻⁴² In addition, Traut and Marchetti⁴³ have reported a series of 54 tumors, four of which were thought to be pure thecomas, one a pure granulosa-cell tumor, and 49 a general admixture of both types.

In recent years, Geist and Gaines,¹² Dockerty,²¹ Wolfe and Neigus,²⁴ Henderson,²⁸ and Novak⁴⁵ have made substantial additions to the literature regarding this gynecologic entity.

Histogenesis

The origin of theca-cell tumor is a subject of considerable controversy. Novak⁴⁵ states that the tumor is derived from embryonic ovarian mesenchyme, having a common origin with the granulosa-cell tumor of which he considers the theca-cell tumor to be a subdivision. This view has been supported by Greenhill and Greenblatt,¹⁴ Traut, Kuder, and Cadden;¹⁸ and Fallas.²⁷

Geist⁴⁴ maintained that the theca-cell tumor is derived from the unused and immature theca cells of the ovarian parenchyma, and therefore is a separate entity from the granulosa-cell tumor. Dockerty²¹ likewise adheres to this theory.

It is not within the limits of this paper to attempt a settlement of these two opposing views.

Clinical Features

Sixty-five per cent of theca-cell tumors occur after the menopause, and thirty-five per cent occur in the period between puberty and the climacterium. The tumor has never yet been demonstrated in children.

Development of theca-cell tumors during the years of normal sexual activity generally results in menorrhagia, often preceded or succeeded

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by a period of hypomenorrhea or amenorrhea. Not infrequently, there are no menstrual abnormalities noted. Varying degrees of virilism have been reported in three instances previously.^{12, 17, 22}

Atypical bleeding is the most prominent symptom in post-menopausal patients. The bleeding may be cyclic or irregular, scanty or profuse. Other changes noted are a rejuvenation of atrophic breast tissue, recrudescence of libido, and a revitalization of the vaginal mucosa.

Physiologically, because of the hyperestrinism produced by the tumor, the uterus becomes enlarged and softened, with a glandular cystic or adenomatoid hyperplasia of the endometrium.

All symptoms abate upon extirpation of the tumor. In the pre-menopausal group, the periods again recur regularly; in the postmenopausal group, the bleeding ceases.

Pathology

The tumor is always unilateral, no bilateral theca-cell tumors ever having been reported. Thecoma tends to simulate the fibroma of the ovary in size, shape, and consistency. A capsule is commonly present. On cut section, the surface is noted to be composed of varying-sized islands having a diagnostic yellow hue and separated by grayish-white fibrous bands. Small cystic areas are an inconstant feature and result from liquefaction necrosis.

Histologically, the tumor is composed of interlacing fasciculi of connective tissue scattered through which are nests of polygonal or large spindle cells having an epithelioid appearance. These latter cells have a dark staining protoplasm and oval-shaped or elongated nuclei which are eccentrically situated. Intercellular and intracellular lipoid is a characteristic feature. Hyaline plaques in the interstitial matrix are also commonly observed.

Material

In the study of 176 ovarian tumors removed surgically on the Kings County division at Kings County Hospital since January 1, 1935, there were 33 solid tumors of which 3 were thecomas. Other dysontogenetic tumors observed in this series were 4 granulosa-cell tumors, 2 dysgerminomas, and one luteoma. One theca-cell tumor in our series was discovered incidentally at autopsy.

All our specimens were fixed in formalin immediately after removal, a fact which has precluded their study for hormonal content. The clinical and histopathological data are sufficiently interesting, however, to warrant the report of these cases.

Case Reports

CASE 1.—The patient, a white, unmarried, 17-year-old female, entered on June 7, 1942 because of a progressive enlargement of an abdominal tumor mass, first noted by her 15 months before. The mass had caused no symptoms other than a swelling of the left lower extremity for 2 weeks before admission. There had been no menstrual irregularities. Her menses had begun at the age of 12, and recurred regularly every 30 days, lasting 4 to 5 days. The last menstrual period had begun May 30, ending June 4. She had noted a 12-pound weight gain during the preceding year.

On examination, no change was noted in the secondary sex characteristics except that the breasts were small and poorly developed. The abdomen contained a very firm, ovoid mass, the size of a full-term gravid uterus, which seemed to almost completely fill the pelvic and abdominal cavities. There was more fullness in the left flank than in the right. A bruit was auscultable in the right lower quadrant. On rectal examination, the uterus and adnexa could not be made out.

On June 15, through a midline incision from the xiphoid process to the symphysis pubis, the right tube and a huge solid tumor which had completely replaced the right ovary were removed. The tumor measured 30 by 25 by 18 centimeters and weighed 5,380 grams (12½ pounds). The uterus and left adnexa appeared normal. A slight amount of clear free fluid was noted in the peritoneal cavity.

Convalescence was uneventful, and the patient was discharged on June 28, 1942.

Since her operation, the patient has maintained good health. Her periods have been regular every 30 days. She has become more feminine in appearance. The breasts have become more developed and full.

Pathologic report: On section, the tumor was found to be completely encapsulated. Cut surface of the tumor was firm and grayish-pink in color, with focal areas of yellow tissue separated by white fibrous bands.

Microscopic examination revealed ovarian tissue being replaced by a neoplasm made up of bundles and strands of interlacing connective tissue. The individual tumor cells varied from a plump ovoid type to a more elongated and flattened spindle-cell type. Special stains showed intra- and extra-cellular lipid in large amounts.

The histopathologic diagnosis was thecoma of the ovary.

CASE 2.—The patient, a 43-year-old colored laundress was admitted on July 17, 1943. One week before admission, she had developed a sharp cramping pain in the left epigastrium, which after 2 days localized in the right inguinal region as a dull, constant ache. There had been no nausea or vomiting. There had been no menstrual irregularities. Her last period two weeks before admission had been normal in all respects. Menses had begun at 13, recurred every 28 days for 4 days. There was no dysmenorrhea. The patient had 1 living daughter, 27 years old. A second pregnancy in 1925 had terminated spontaneously in an abortion at 3 months' gestation.

Physical examination on admission was essentially negative except for moderate tenderness in the right inguinal region, just above Poupart's ligament. No rigidity was present. An irregular mass was palpable, rising out of the pelvis.

On pelvic examination, motion of the cervix caused pain in the lower abdomen. The uterus was irregularly enlarged to 4 months' gravidity, firm, drawn to the right, anterior, tender to palpation, and somewhat fixed to motion. Both fornices seemed indurated and tender to palpation.

The clinical impression was myomata uteri with chronic pelvic inflammatory disease.

At operation on July 23, the small bowel showed acute congestion, edema, and some exudate; and the loops were intimately adherent to each other and to the omentum which was also acutely congested. The appendix, which was in the center of the congested area, also showed acute congestion. The left ovary was completely replaced by an orange-sized,

moderately firm tumor, the pedicle of which was twisted two complete turns. The tumor on cut section showed cystic degeneration with focal areas of infarction. Several islands of yellowish-white tissue were noted. The right ovary contained a small firm nodule, $2\frac{1}{2}$ centimeters in diameter, which on cut section appeared composed of whorls of white fibrous tissue. The uterus was the seat of intramural and subserous fibroid tumors.

A supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed. An appendectomy and partial omentectomy were also completed.

Postoperative convalescence was uneventful, and the patient was discharged on the twelfth postoperative day. Except for menopausal symptoms, her general health has since remained good.

Microscopic study of sections of the left ovary showed a neoplasm composed of elongated and plump spindle cells growing diffusely and arranged in bundles. In many areas, the tumor was loosely textured. Many of the cells showed vesiculation, with the cytoplasm and also the interstitial matrix showing vacuolization and clear spaces. Numerous varying-sized cysts and areas of interstitial hemorrhage were scattered throughout. Sudan III stains revealed numerous collections of lipid scattered intra- and extra-cellularly. The endometrium appeared in the late proliferative phase of the menstrual cycle.

Final histopathologic diagnosis was thecoma of the left ovary with focal hemorrhagic infarction, fibroma of the right ovary, myomata uteri, salpingitis isthmica nodosa, and chronic appendicitis with acute peritoneal reaction.

CASE 3.—The patient was a 52-year-old white housewife who had been under treatment of a local physician for one year for menopausal symptoms. Her periods had been recurring irregularly during this time. She was admitted to Kings County Hospital on January 27, 1941 because of mental confusion and disorientation of 4 days' duration. Signs and symptoms were those of cerebral damage due to multiple vascular lesions. Treatment was supportive, but the course was rapidly downhill and the patient expired on February 26, 1941.

Autopsy revealed a meningioma of the left frontal lobe, generalized arteriosclerosis, and medullary fibrosis of the kidneys.

An incidental finding of an encapsulated tumor mass, $1\frac{1}{2}$ centimeters in diameter, was noted in the medullary portion of one ovary. Microscopically, this tumor was composed of broad spindle-cells distributed in an irregular, interlacing fashion. Sudan III stains revealed intra- and extra-cellular lipid in considerable amounts. Foote silver stains and van Gieson stains confirmed the diagnosis of thecoma. Endometrial sections were not available, although several small intramural myomas were noted in the uterus.

CASE 4.—The patient, a 52-year-old Negro widow, entered the hospital on October 6, 1943 with the chief complaint of vaginal bleeding. The patient had been amenorrheic since her menopause in 1940, except for the appearance of a profuse, painless vaginal bleeding 3 weeks before admission, which persisted. She had borne one child. Menses had recurred regularly every 28 days prior to onset of her menopause.

Pelvic examination revealed a short firm cervix with an irregularly enlarged and nodular uterus filling the pelvis.

A supravaginal hysterectomy and right salpingo-oophorectomy were performed on October 13 for myomata uteri and a right ovarian tumor. Left ovary and tube appeared normal grossly. Attached to the median pole of the right ovary by a short pedicle was a soft, rubbery, walnut-sized, yellowish-tan nodule. Section of this revealed a homogenous yellow, glistening surface. Section of the uterus revealed numerous intramural and subserous fibroids with one small submucous nodule in the fundus showing degenerative changes.

Postoperative course was uneventful, and the patient was discharged on the tenth postoperative day. General health has remained good since operation.

Microscopic study of the tumor revealed a neoplasm composed of elongated and plump spindle-shaped cells, showing a striking tendency to be arranged in bundles and whorls, the former frequently interlacing with one another in an irregular fashion. In many instances the cells showed vesiculation, with the nucleus eccentrically displaced. In some instances, the cells appeared to be ovoid or spheroidal and epithelial-like in nature, having a scanty or clear cytoplasm. The tumor for the most part was compact and solid, although occasional areas were noted where the stroma was light textured and reticulum-like, with the cells stellate in type. With the van Giesen stain, the neoplasm seemed to be composed predominantly of young fibroblastic tissue and collagen fibrils. With Sudan III stain, a large quantity of fat was seen throughout the tumor, located both intra- and extra-cellularly in the form of globules and droplets.

The endometrium showed moderate hyperplastic changes with occasional fibroblastic changes and round-cell infiltration. In some areas the glands were dilated and cystic in type. One area proved to be a submucosal fibromyomatous neoplasm which had undergone extensive superficial hemorrhagic infarction.

Final histopathologic diagnosis was myomata uteri, chronic hyperplastic endometritis, and thecoma of the right ovary.

Discussion

In seventy-four cases collected from the literature having data sufficient for statistical purposes¹⁻³¹ and including our four cases, the age incidence was as follows:

| | |
|------------|----|
| 15 to 19 | 3 |
| 20 to 29 | 7 |
| 30 to 39 | 8 |
| 40 to 49 | 8 |
| 50 to 59 | 28 |
| 60 to 69 | 12 |
| 70 to 79 | 5 |
| 80 to 89 | 0 |
| 90 to 95 | 1 |
| Not stated | 2 |

It is to be noted that 28, or 37.83 per cent, of these tumors occurred in the 50 to 59-year age group. Postmenopausal appearance of the tumor was noted in 64.86 per cent. Postmenopausal bleeding was present in 72.92 per cent.

The youngest patient having a thecoma was 16 years of age; the oldest was 92. The average age was 50.62 years.

The size of the theca-cell tumor presumably bears no relationship to its endocrine function. In the first case reported by us, no menstrual irregularities were noted by the patient despite the fact that the tumor was extremely large and weighed 5,380 grams, the largest yet reported. Generally, the tumors are no larger than a hen's egg, although some have been reported to attain the size of a small melon. Dockerty²¹ reported one tumor, found incidentally at biopsy of a surgical specimen, which measured only 2 millimeters in diameter. A number of tumors ranging between 1 and 3 centimeters in diameter have been reported. Only a few large tumors have ever been reported. Voight²⁰ in 1940 reported a theca-cell tumor weighing 7 pounds (3,180 grams), also removed surgically. The tumor in this latter case produced irregular menses with scanty flow in a 36-year-old nulligravida.

Traut and Marchetti⁴³ have suggested that the endocrine activity of theca-cell tumors is lessened by lack of differentiation of the tumor, the presence of a high theca-cell content, or by senescence of the tumor in association with marked fibrosis and other degenerative changes.

In one of our cases, we found infarction of the theca-cell tumor as a result of torsion of the tumor pedicle. Torsion was also noted in 5 of 8 cases reported by Wolfe and Neigus.²⁴

Likewise, free peritoneal fluid is occasionally observed with theca-cell tumors. We observed it in one case. A total of seven other examples have been recorded in the literature by Loeffler and Priesel,^{1, 2} Geist and Gaines,¹² Donisi,¹⁹ Dockerty,²¹ and Wolfe and Neigus.²⁴ The case reported by Loeffler and Priesel proved to be a malignant thecoma with evidence of metastases. The other cases were all benign tumors, and there was no recurrence of the ascitic fluid after removal of the tumor.

Of 46 cases in the literature reporting endometrial findings, 36 showed hyperplastic changes, 32 of which were in the postmenopausal group. Atrophic endometrium was demonstrated twice, while normal endometrium was encountered 3 times. There were 5 examples of an associated endometrial carcinoma, all in the postmenopausal group. The association of carcinoma with theca-cell tumors suggests the question of carcinogenic properties of estrin.

Of 52 cases in which a description of the uterus was given, 24 cases of theca-cell tumors of the ovary were associated with myomas of the uterus. Hypertrophy of the uterus was noted in addition in 17 cases. Adenomyosis was reported in 5 cases. There were 11 cases in which the uterus was considered normal or even smaller in size.

Theca-cell tumors have also been noted to occur in combination with other ovarian tumors, especially cysts of various types. One of our tumors was noted to be in association with a fibroma of the opposite ovary. Patterson and McCullagh⁵ observed a similar instance in their patient, a 92-year-old female with a thecoma in one ovary and a fibroma, one inch in diameter, in the opposite ovary.

Geist and Gaines¹² stated that no relationship could be drawn, however, between theca-cell tumors and the uterine fibroids or ovarian cysts coincidentally found with them.

To date, there have been only three cases of malignant theca-cell tumors reported. These have been thoroughly described by Loeffler and Priesel,¹ Huber,⁷ and Geist and Gaines.¹²

At the most, theca-cell tumors are a form of low-grade ovarian malignancy. Most surgeons feel that treatment need not be radical, a simple excision of the ovary being sufficient in the vast majority of cases. Theca cells are considered to be radioresistant, so that radiation therapy is generally considered to be of little or no value except for the diminution of the size of the tumor by the effect of x-ray on the fibrous tissue stromal elements.

Summary

Four additional examples of theca-cell tumors of the ovary have been reported, three being removed surgically, one having been discovered incidental to autopsy. All the tumors were benign. One very large tumor occurred in a 17-year-old girl, producing no menstrual irregularities. One tumor associated with a fibroma of the opposite ovary showed infarction due to torsion of its pedicle. Convalescence and follow-up of the three cases have been uneventful.

A complete summary of the literature has been presented.

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55 EIGHTH AVENUE

451 CLARKSON AVENUE

POSTMENOPAUSAL OVARIAN CARCINOMA

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THE "silent" ovarian tumor has long been recognized as a great menace in the control of cancer by early recognition and treatment. The new growth is either discovered accidentally, in the course of a routine pelvic examination, or when the tumor becomes extensive enough to be noticed by the patient or to cause pressure symptoms, at which time it is usually beyond surgical interference. In a discussion of this subject, H. S. Crossen¹ suggested, among other things, "insistence on regular periodic pelvic examinations of patients who ask the physician to assume responsibility in regard to their health. These periodic examinations for silent ovarian carcinoma should be made every six months, instead of once yearly, which was formerly supposed to provide adequate safety." This is excellent advice. While it may require a great deal of educational propaganda to convince the average private patient as to the importance of such frequent examinations, it should not be difficult to institute such a routine among clinic patients. With a proper follow-up system, the patient can be instructed when to report, and is sent for if she fails to do so.

However, even among the members of the medical profession, the importance of these frequent examinations has as yet not been fully realized. Only too frequently a patient is discharged as cured or improved without any instructions to report to the clinic again for further observation. This is especially true of a group of patients with irregular menopausal bleeding. This type of patient is usually sent in to the hospital for a diagnostic curettage and insertion of radium. If the examination of the curettings fails to reveal any malignancy, a castration dose of radium is applied. The patient may subsequently be seen in the clinic for a few months and, if there are no further complaints, she is discharged as cured with instructions to report in case of any recurrence of bleeding or staining. But, the fact that a patient received radium treatment for benign menopausal bleeding does not insure her against the development of other pelvic pathology even in the absence of bleeding. This was brought out by Pemberton² who, in a series of 86 cases of postmenopausal ovarian malignancy, described two patients who had previously received radium for benign menopausal bleeding. Neither of these patients had any palpable ovarian pathology at the time she was treated with radium.

It was in order to further emphasize this point that it was deemed advisable to report the following case.

Case Report

M. R., a 56-year-old white female, was admitted to the Beth Moses Hospital on April 21, 1941, complaining of irregular vaginal staining and bleeding for the past two months. There were also occasional attacks of dizziness and a loss of eight pounds in weight.

Menses started at the age of 13, occurring every 28 to 31 days and lasting 4 to 5 days. The patient had two stillbirths, one of 7 months'

gestation 30 years previously, and one of 8 months' gestation 28 years ago. She had one normal pregnancy and delivery at term 26 years ago. Her last menstrual period was three years ago. There was no staining or bleeding until the time of her present illness.

Abdominal examination did not reveal any rigidity, tenderness or palpable masses. Vaginal examination showed a multiparous outlet. The cervix was hard, lacerated, eroded, not friable and freely movable. The uterus was slightly enlarged, anteverted and deviated to the left, movable and not tender. The adnexa could not be palpated.

A diagnosis of possible malignancy of the corpus uteri was made and a diagnostic curettage was advised. This was done on April 22, 1941. Only a small amount of tissue was obtained in spite of thorough curettement. The pathologic report was that of shreds of endometrium and myometrium with no evidence of malignancy. The patient was discharged from the hospital at the end of a week.

The bleeding and staining persisted and the patient was readmitted to the hospital on September 8, 1941. The vaginal findings were the same as on her previous admission. Another curettage was performed and 50 mg. of radium were inserted in the uterine cavity. The pathologic diagnosis of the curettings was that of cervical epithelium and myometrium. There was no evidence of malignancy.

The patient received 1,950 millicurie hours of radium. She left the hospital on September 21, 1941, in good condition. There was no further bleeding or staining and after the third monthly visit to the clinic, the patient was told to report only in case of any further complaints.

During May, 1942, the patient was readmitted to the hospital for an hemorrhoidectomy. A vaginal checkup at the time disclosed a hard lacerated cervix, a small uterus, freely movable. The adnexa could not be palpated.

The patient was not seen again until February, 1944, when she returned to the gynecologic clinic complaining of pain in the left side of the lower abdomen for the past six weeks. The pain was constant, dull in character, radiating down the left thigh and leg. She suffered from frequent and urgent micturition. She was constipated and felt bloated. There was no loss of weight. Abdominal examination showed the presence of a moderate distension but there was no evidence of fluid. An irregular, fixed mass could be felt above the symphysis, apparently arising from the pelvis. Vaginal examination revealed the presence of a hard mass filling the region of the left fornix and the posterior cul-de-sac. The cervix was hard, closed and movable. The uterus could not be felt separately from the mass. The right adnexus was hard and thickened. A diagnosis of pelvic malignancy was made with the possibility of intestinal malignancy to be excluded. She was admitted to the hospital on March 2, 1944. A radiographic study of the colon by means of a barium enema showed a spastic sigmoid with a soft tissue mass in the pelvis, which appeared extracolonic.

The patient's blood pressure was 130/90. The hemoglobin was 13 mg. per 100 c.c. of blood. Red blood cells were 5,190,000; white blood cells 19,000; polymorphonuclear leucocytes 72 per cent; lymphocytes 28 per cent. Blood Wassermann and Kahn tests were negative. Blood sugar was 90 mg., and urea nitrogen was 15 mg. per 100 c.c. of blood. Repeated examinations of the urine were essentially negative.

On March 6, 1944, a laparotomy was performed under spinal anesthesia. Upon opening the peritoneal cavity the following was noted:

There was a mass, the size of a grapefruit, in the left side of the pelvis, firmly adherent to the omentum, sigmoid and pelvic floor. This mass seemed to include the uterus and ovary, neither of which could be separately identified. The right ovary was enlarged, adherent to the intestines and posterior layer of the broad ligament and contained sero-sanguineous fluid. A supracervical hysterectomy and bilateral salpingo-oophorectomy were performed.

The following were the pathologic findings of the specimen, as described by Dr. A. R. Kantrowitz:

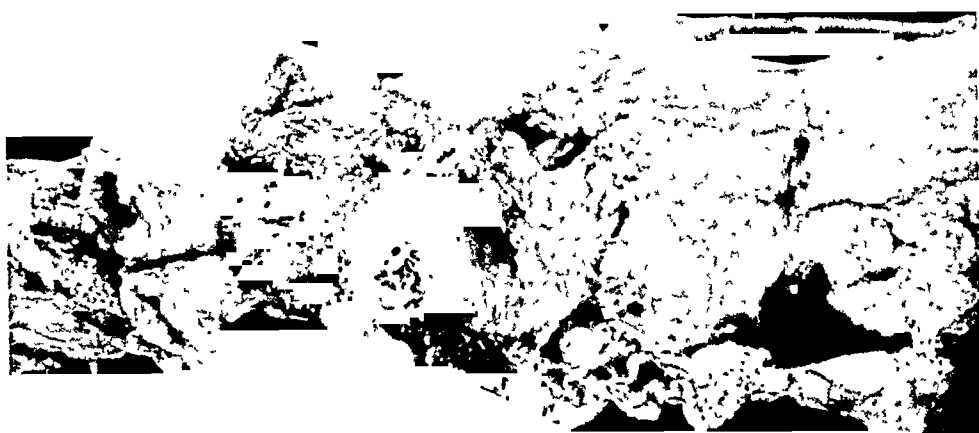


Fig. 1.—Gross specimen showing body of the uterus in the center, firmly adherent to the large left ovarian mass, and smaller right ovary.

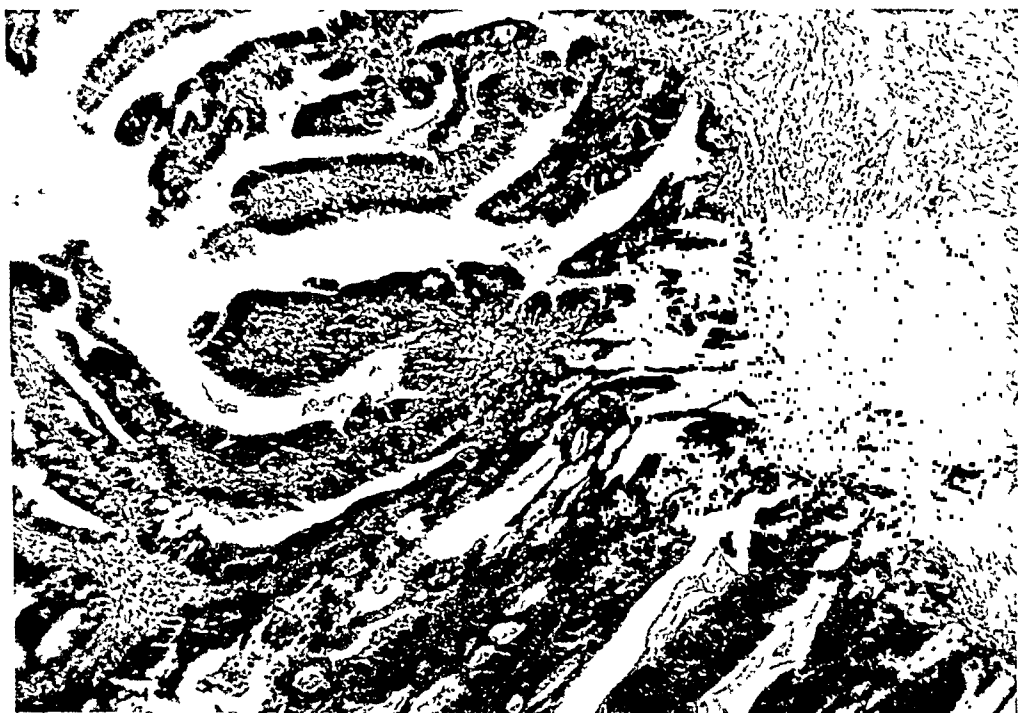


Fig. 2.—Section of left ovary consisting of papillary and glandular structures, lined by cuboidal to polyhedral cells showing marked atypism with numerous mitoses and giant cells. ($\times 75$.)

Gross.—Specimen consists of a supracervically amputated uterus, together with both tubes and ovaries. The uterus is bound by dense adhesions to a large left ovarian mass. The uterus measures 6 by 7 by 5 cm. The surface is markedly roughened by the presence of numerous connective tissue tabs. The uterus is considerably distorted because of the presence of numerous masses situated within all locations. The endometrial cavity cannot be probed. Cross section reveals chocolate-brown tissue replacing the cavity completely, except in one small area at the left fundus.

The right tube measures 10 cm. in length; its fimbriated end is patent. The ovary is enlarged and measures 7 by 3 by 3.5 cm. The surface of the right tube and ovary is covered with very dense adhesions.

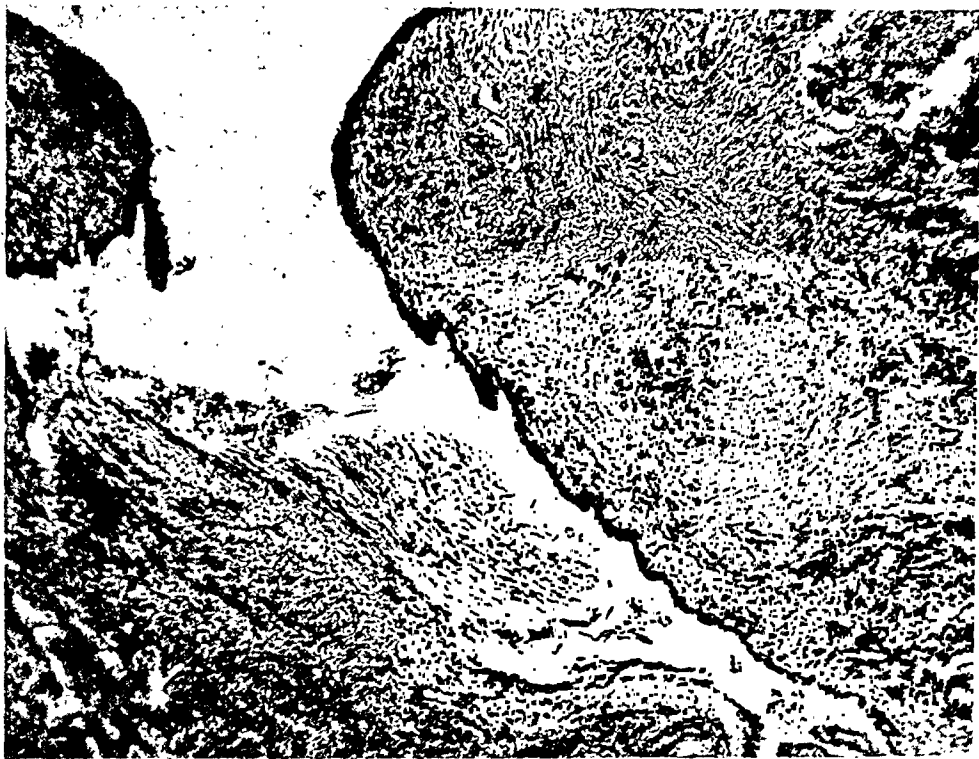


Fig. 3.—Section of uterus showing almost complete atrophy of the endometrium and its replacement by scar tissue in some areas. ($\times 75$.)

The left ovarian mass measures 9 cm. in diameter. The entire mass consists of yellow tissue presenting a necrotic appearance. It is bound by dense adhesions to the uterus, the wall of which is invaded by the yellow amorphous tissue at the area of attachment.

Microscopic.—The endometrium is atrophic and the cavity, in its greatest extent, is replaced by scar tissue with pigment-laden macrophages. The myometrium is invaded by nests of atypical polyhedral cells in a few areas.

The left ovarian mass consists of papillary and glandular structures lined by cuboidal to polyhedral cells showing marked atypism with numerous mitoses and giant cells. The greater portion of the mass is completely necrotic. The cyst locules are lined by similar cells. The right ovary contains nests of identical cells.

Diagnosis: Bilateral papillary cystadenocarcinoma of the ovaries with extension to the uterus. Status after radiation of the uterus: Obliteration of the endometrial cavity; myomata of the uterus.

The patient made an uneventful recovery except for a complicating cystitis. This condition responded to sulfonamide therapy and bladder irrigations. She was discharged from the hospital on March 31, 1944, in good condition.



Fig. 4.—High power of section of uterus showing invasion of myometrium by atypical polyhedral cells. ($\times 335$.)

Comment

This case presents a few interesting points worthy of note. The castrating dose of radium, which was given to the patient in order to suppress the activity of the ovaries and secondarily eliminate their proliferating influence upon the endometrium, had its desired effect. This is evidenced by the atrophy and almost complete absence of the endometrium as shown in the specimen removed, and by the cessation of bleeding, clinically. However, the irradiation had no inhibiting effect upon the later development of a neoplasm in these ovaries. It is important to bear in mind the possibility of such a consequence in a postmenopausal patient who had received radium treatment for bleeding and is apparently cured. Such patients, as well as others under observation, should be examined at frequent, regular intervals for any pelvic pathology. Had the patient reported here been examined more frequently, the growth may have been discovered before it became so big, adherent to the adjacent tissues, and extended into the uterus. Surgery would have been resorted to at an earlier stage with the probability of a better prognosis.

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LATE RECURRENCE IN CARCINOMA OF FUNDUS UTERI*

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THIS case shows an unusual combination of treatment by radiation and complete hysterectomy in that the radiation was administered nine years and repeated four years preceding operation without any apparent impairment of the result. The patient is enjoying good health today, exactly six years after hysterectomy. The rate of five-year survival is high following total abdominal hysterectomy.

Masson¹ in a review of the Mayo Clinic cases from 1910 to 1938, found 67.5 per cent where the operation was combined with radiation and 66.6 per cent where radiation was omitted. A review of corpus carcinoma treated by radium alone reported by Fricke and Bowing² in the same institution running from 1925 to 1935 showed a five-year salvage rate of 39 per cent.

In the series of cases reported recently by Sheffey, Thudium and Farrell,³ their five-year salvage by operation without radiation was 36.3 per cent, and with radiation alone 40.5 per cent.

Complete operation following preliminary treatment with radium, gave these authors the higher five-year salvage rate of 42.9 per cent.

Outstanding five-year results of this combined form of therapy have been reported by Miller⁴ 82.3 per cent, Smith⁵ 66.2 per cent, Ward⁶ 64.9 per cent, and Healy and Brown,⁷ 55 per cent.

At the time this patient was radiated, she was not considered suitable for operation due to previous nephrolithiasis and recurrent pyelitis in her only remaining kidney.

These conditions had ameliorated sufficiently by the time her vaginal bleeding recurred in 1938, so that complete abdominal hysterectomy had become practicable.

In cases which fell roughly into the group of unsuitable operative risks, such as this patient was in 1929 and in 1934, radiation alone has given some interesting five-year salvage in various series, Norris and Dunne⁸ reported 43.8 per cent, Healy and Brown,⁷ 39 per cent and Ward,⁶ 32 per cent.

Previous to 1938, she had been under the care of a surgeon in her home community, and was referred to me only for operation.

The history is briefly as follows:

Mrs. N. R., aged 54, white, married, admitted March 4, 1938. *Chief complaint:* Vaginal bleeding over a period of 10 years.

Past History: Right nephrectomy, twenty-four years previously for calculus. Left pyelotomy, seventeen years previously for calculus. Found to be hypothyroid eight months ago, and takes thyroid intermittently.

Present History: Twenty-four years before admission, following birth of last child at the age of 30, regular menstruation ceased. Nine years prior to hospitalization, i.e., in April, 1929, at the age of 42, she de-

*Presented at a meeting of the New York Obstetrical Society, March 14, 1944.

veloped severe vaginal hemorrhages and was curetted for diagnosis, revealing a malignant adenoma. Treatment with radium, 50 mg. screened with 1 millimeter brass and 1 millimeter of rubber for 48 hours.

In July, 1934, treated again with radium for spotting. Fifty mg. as above for 24 hours. October, 1937, bleeding recurred and for past week has been profuse. She was advised to have a complete hysterectomy with bilateral salpingo-oophorectomy, which was performed March 7, 1938 under general anesthesia.

Physical Examination: Obese elderly woman. Blood pressure 140/84. Abdomen extremely obese. Small well-healed scars of bilateral renal operations. Otherwise essentially negative. Her uterus was reported as of normal size in 1929, but to have increased considerably in size by January, 1938.



Fig. 1.—Section of curettings taken in 1929, when first irradiated. Diagnosis: Adenoma malignum.

Operation: At operation considerable difficulty was encountered in getting hemostasis of left uterine artery, but transfusion was not necessary. Postoperative course was uneventful except for a recurrence of the old pyelonephritis, which subsided under medical treatment. Left hospital on sixteenth postoperative day.

Pathological Report: Uterus complete, size, 3 by 1½ by 1½ inches with both tubes and ovaries attached. Outer surface smooth. When opened, the entire fundal region is covered with an ulcerating and fungating growth about half an inch in elevation. Tubes appear small and normal. Both ovaries are sclerotic and fibrocystic in character.

Microscopic Examination: Sections of uterine wall show the surface endometrium replaced by a typical glandular overgrowth. The glands are large, irregular, tortuous and lined by elongated columnar epithe-



Fig. 2.—Curetings, 1934, irradiation for vaginal bleeding.



Fig. 3.—Curetings, 1938. Diagnosis: Adenocarcinoma of fundus uteri.

lial cells. There is moderate infiltration of the superficial endometrium. The ovaries are sclerotic and contain scattered small follicular cysts.

Diagnosis: Adenocarcinoma of fundus; sclerotic ovaries.

I am indebted to Dr. Herbert B. Gibby of Wilkes-Barre, Pa., for the details of findings and treatment before March, 1938.

130 EAST 56TH STREET

Discussion

DR. WILLIAM E. STUDDIFORD.—The case reported by Dr. Barrows is of interest from several points of view.

This patient ceased menstruating at the very early age of 30 and did not develop symptoms of carcinoma until she was 45 years of age, which is an early age for most cases of carcinoma of the corpus. Nevertheless, the interval between the cessation of menstruation and the time of the development of clinical symptoms of carcinoma is approximately the same as that noted in patients who usually cease to menstruate at about the age of 50.

The question arises as to whether this neoplasm represents a recurrence of the original tumor, or the appearance of a second carcinoma, possibly influenced by radiation therapy, a sequence. In favor of the latter theory is the fact that the patient was curetted midway between the two occasions when carcinoma was found and the curettings appeared to be benign, at least negative for carcinoma. On the other hand, it is a very well-known fact that radium is quite often ineffective in cases of carcinoma of the corpus and simply serves to coat the surface of the tumor with a layer of tissue which becomes hyalinized and necrotic, and this layer serves to stop bleeding and so mask the continued presence of the tumor.

I do not believe that there is very much question that the most likely explanation of the course of Dr. Barrows' case is that the original tumor must have been masked by the radiation therapy, and the patient subsequently developed further evidences of carcinoma of the corpus, resulting in her final operative treatment.

The most logical conclusion that one can draw from this case is that all patients with carcinoma of the corpus uteri treated with radiation should be subjected to total hysterectomy and bilateral salpingo-oophorectomy, provided the contraindications to such an operation are not too great. Dr. Barrows has certainly demonstrated that the contraindications to operation in this case were not too great under our present methods.

DR. HOWARD C. TAYLOR, JR.—After reading Dr. Barrows' case report several days ago, I looked up a series of cases that we had once studied which showed the intervals between the first diagnosis of carcinoma of the corpus uteri and its final operation. I found one case in the series which had a hysterectomy at 61, and had been curetted at 45. The original diagnosis in this case was papillary adenoma of the endometrium and was regarded at that time as benign. Consequently the operation had been a simple curettage. When the sections were reviewed, it was found that the original lesion had exactly the same appearance as that found sixteen years later. This then was a patient who had a curettage for adenoma malignum without radium, and finally sixteen years later had a hysterectomy for an adenoma malignum. I think it is quite possible with this type of growth for the cancer to last sixteen years without interference by radium. The point is simply that this may be a very slow growing type of tumor.

The proper treatment of carcinoma of the corpus is certainly hysterectomy if the patient can stand the operation. Dr. Barrows' case, I understand, was one which was assigned to radium because she was considered a poor risk and yet the operation was carried out 11 years later when the risk was definitely poorer. In a patient of

60 with a carcinoma of the corpus, unless her medical status is extremely bad, it is much better to take your risk then than to wait ten years more and take a much greater risk when the possibilities of radiation have been exhausted and the patient must face an inevitable hysterectomy.

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RECURRENT TUBAL PREGNANCY IN TUBERCULOUS SALPINGITIS*

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TUBAL pregnancy is by no means an unusual entity nor is tuberculous salpingitis. The combination of these two, however, according to Wharton and Stevenson¹ is one of the rarest combinations seen. These two authors first called attention to this in 1939 with a case report and a survey of the entire literature. They found only eight cases of proved coincidental tuberculous salpingitis and tubal pregnancy in the world literature, and reported the first case in the English literature. In addition to these cases, they found eight cases in which the gestation sac lay completely or partly free in the abdominal cavity. In three cases, the gestation sac lay cradled in the fimbria of one tube, and in five cases found the sac entirely outside the tube in the abdominal cavity. This indicates a striking incidence of abdominal pregnancy, for fifty per cent of ectopic pregnancy in the presence of tuberculous salpingitis were abdominal pregnancies. This is apparently due to failure of the fertilized ovum to enter or find nidation in the tube.

Again to emphasize the rarity of this combination, Stevenson and Wharton² stated that in 46,700 specimens submitted to their gynecologic pathologic laboratory, there were 402 cases of tuberculous salpingitis and 516 cases of tubal pregnancy, and their case was the first to combine these two entities. Bland,³ in 1940, reported that from 1928 to 1939 in the laboratory of the Jefferson Medical College, there were operated upon 193 cases of various forms of extrauterine pregnancy, or nearly 20 cases each year. None of these showed any evidence microscopically of tuberculous infection of the tubes. At the Elizabeth Steel Magee Hospital from June, 1928, to June, 1943, or a 15-year period, there were 12,841 gynecologic operative procedures. Among these, there were 32 cases of tuberculous salpingitis and 154 tubal pregnancies, but no combination of the two. There were 20,873 pathologic specimens submitted to this laboratory during this time from all services (gynecology, obstetrics and surgery) without a case of tubal pregnancy in a tuberculous tube.

Since the report by Stevenson and Wharton,² cases have been reported by Stein,⁴ Busby and Fisher,⁵ Bland,³ and Shannon and Heller⁶ in American journals. Rojel⁷ and Hicks⁸ have each reported a case in foreign journals not available. The case of Shannon and Heller⁶ was quite unusual in that a five- to six-month intratubal gestation was found at autopsy.

*Presented at a meeting of the Pittsburgh Obstetrical and Gynecological Society, April 3, 1944.

Wharton and Stevenson¹ have discussed the pathology in detail and offer as reasons for the infrequency of this combination the fact that tuberculosis is an invasive destructive disease with resultant (1) obstruction of lumen of the tube to any passage of any sperm or ova; (2) lack of nutrition from diseased tubal mucosa to transient fertilized ova; and (3) lack of tubal mucosa healthy enough to allow successful nidation of the fertilized ovum if it is trapped in the tube.

This case report is being presented because of the rarity of this combination of pathology and because it is, as far as I can determine, the first case in which there has been a recurrence of this unusual entity.

Mrs. C. F., 35 years old, white, was admitted to the Woman's Hospital of Pittsburgh, on November 7, 1943, at 4:00 P.M. with chief complaint of severe pain in the lower abdomen. Pain began immediately after lunch, suddenly and sharply in the lower abdomen on the left side. Nausea and vomiting were associated with this and pain has persisted with acute exacerbations. There is a feeling of pressure in the rectum and pain deep in the pelvis. Two weeks previously, patient had a similar attack but much less severe. Last menstrual period was September 12, 1943. She has missed her October period and this is the expected date of her November period. She has had slight spotting a few days ago which lasted for a few hours, but which has started again since the onset of pain. Patient began menstruating at the age of twelve, has been regular every 28 days, periods lasting four to six days. In October, 1941, patient had a ruptured tubal pregnancy on the right side which was operated upon at this hospital. Information obtained from the old chart of the microscopic examination of this tube revealed a tuberculous salpingitis in addition to the ruptured ectopic pregnancy. Patient has never had active tuberculosis that she is aware of and has never been bedfast or placed in any sanatorium. She has had x-rays of her chest, but no comment was made on this. Her family physician informed me that four to five years ago her chest had been x-rayed and old healed tuberculosis was found without any evidence of activity. Patient has been married for five years and has never had any abortions or intrauterine pregnancies. She has gained 20 pounds since her operation two years ago. Remainder of history is essentially negative.

Patient on admission appeared pale and in acute distress. Skin somewhat cold and slightly moist. Temperature 98.2° F., pulse 100, respirations 22, blood pressure, 100/60. General physical examination essentially negative. Careful examination of the chest reveals no râles or rubs. There is marked tenderness in the lower abdomen, particularly on the left side, and slight distention. There is rebound and percussion tenderness present. Peristalsis active.

External genitalia negative. Catheterized urine clear. Skene's and Bartholin's glands negative. Cervix clean. Patient is so tender on bimanual examination that no definite bimanual pelvic can be done. However, there is severe and exquisite tenderness in the cul-de-sac.

November 7, 1943, R. B. C. 3,720,000; W. B. C. 13,600; Hb. 74 per cent. Catheterized urine negative. Sedimentation rate, over 90 minutes.

Diagnosis: Ruptured tubal pregnancy, left tuberculous salpingitis.

At 6 P.M. under ethylene, oxygen, local anesthesia, left salpingo-oophorectomy was performed.

The findings at operation were as follows: The left tube was markedly swollen, and in this area was a large rupture in the tube through which protruded a blood clot and placental tissue, and an intact fetus within its amniotic fluid and membrane. The fetus measured 1.5 cm. in length. There was approximately 500 c.c. of free blood in the peritoneal cavity. The left tube was attached to the broad ligament by fine fibrous adhesions; the ovary was not identified. The uterus was enlarged to about the size of a six to eight weeks' gestation, was soft and boggy in consistency and purplish in color. There were numerous small fibroids present in the uterine wall. The uterus was in second degree retroversion, and was bound to the cul-de-sac by fine fibrous adhesions. The right tube and probably the right ovary had been removed at a previous laparotomy, and were not palpated or seen. The omentum was adherent to the anterior abdominal wall at the site of previous laparotomy. In view of the patient's general condition and the amount of hemorrhage sustained, although hysterectomy was felt necessary, it was deemed inadvisable to perform it at this time.

The pathologist reported on the specimen: "tuberculous salpingitis with tubal pregnancy, corpus luteum of left ovary." Re-examination of the specimen from the previous operation revealed the same pathology.

Patient had an uneventful postoperative convalescence, the temperature never rising over 100° F., coming down to within normal limits by the seventh postoperative day and remaining so until the time of discharge.

November 18, 1943, x-ray of chest: The heart and great vessels are normal. There is a very extensive calcification throughout both upper lobes. Much of this consists of calcified nodules but there are also some flat calcified plaques on the right side which are apparently in the pleura. These changes undoubtedly represent an old tuberculosis. There is nothing suggestive of present activity.

November 11, 1943—R. B. C. 3,000,000; W. B. C. 8,800; Hb. 68 per cent.

Patient was discharged November 21, 1943, in good general condition. The wound was well healed and the patient offered no complaints.

December 28, 1943. Patient feels quite well and states that she feels much better than she has in the last few years; has gained six pounds in weight since operation; has had no vaginal bleeding. There have been no hot flushes. Abdominal wound is well healed. Pelvic examination: External genitalia negative. Cervix clean, uterus small and fixed anteriorly. There are no masses palpable in the pelvis and no tenderness. Endometrial biopsy disclosed a tuberculous endometritis.

The diagnosis in this case was not difficult as the picture of a ruptured ectopic pregnancy was quite typical. The history of a previous tuberculous salpingitis in the right side made us aware that this undoubtedly was present also on the left side.

In view of the fact that tuberculous endometritis occurs in about 50 to 60 per cent of cases of tuberculous salpingitis, this was also felt to be a possibility. However, in view of the patient's general condition at the time of operation and the considerable technical difficulties which would have been involved in a hysterectomy, it was felt inadvisable to attempt hysterectomy. Because of the marked adhesions between the tube and ovary, the general condition of the patient, and her age, it was felt wiser to remove both tube and ovary than to attempt the somewhat tedious dissection in order to save the ovary.

Subsequent biopsy has proved that this patient has a tuberculous endometritis. However, since the patient shows definite evidence of having healed her pulmonary tuberculosis, it is quite possible that she may be able to heal the endometrial tuberculosis without necessitating further surgery. At any rate, she is to be watched very carefully in the future and is being placed under the usual medical regime for tuberculosis.

NOTE: Since the date of submission of this article, another case has been reported by Mann and Meranze, *AM. J. OBST. & GYNEC.* 47: 707, 1944.

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MEDICAL ARTS BUILDING

FULL-TERM PREGNANCY AFTER REMOVAL OF REMAINING OVARY AT FIVE MONTHS OF GESTATION*

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THIS report deals with an interesting obstetric complication, namely, a twisted pedicle ovarian cyst at fifth month of gestation followed by full-term delivery in a patient having had a previous oophorectomy. Although many major and minor operations have been successfully performed upon gravid women and pregnancy has continued, according to available literature, only 43 cases of bilateral dermoid cysts complicating pregnancy have been reported. The following case report should serve to add evidence to the belief that neither the ovary nor the corpus luteum play any role in the progress of fetal life after the fourth month of intrauterine development. It is well known, that the hormone secretions of the placenta at this stage of gestation are fully able to maintain the fetus.

Case Report

On April 24, 1940, Mrs. B. K., aged 27, para 0, was admitted to the Jewish Memorial Hospital. The chief complaint was right-sided lower abdominal pains for two weeks prior to admission.

General and laboratory examinations were essentially negative, menstrual history normal, her last period having commenced on March 19, 1940.

Vaginal examination revealed the presence of an irregular cystic mass in the right adnexal region, and a smaller cystic mass in the left fornix. A diagnosis of bilateral ovarian cysts was made. The following day the patient was operated upon. An ovarian cyst, the size of a tangerine, five centimeters in diameter was found on the right side. The left ovary was carefully examined and found to be somewhat larger than normal, the size of a walnut. The right ovarian cyst was excised and the pathology report by Dr. A. Angrist revealed the specimen to be a cyst measuring $4\frac{1}{2}$ cm. in diameter, covered by smooth, glistening peritoneum. On section the cyst contained sebaceous material and hair. The wall itself was rather thin. Microscopic section showed the cystic space to be lined by stratified squamous epithelium with marked keratinization and the outer lining to be of ovarian tissue. The diagnosis of dermoid cyst was made. The uterus and tubes were normal. The patient made an uneventful recovery and was discharged from the hospital two weeks after operation.

On May 21, 1941, thirteen months after the original operation, the patient was delivered by Dr. Warner of a normal, living male infant, 6 pounds, 7 ounces. It was a spontaneous delivery, L.O.A. after 7 hours of labor. A right lateral episiotomy was performed and the post partum was normal.

*Presented before the section of Gynecology and Obstetrics at the New York Academy of Medicine, New York City, on February 28, 1944.

On January 25, 1943, twenty months after the first delivery, the patient was again admitted to the Jewish Memorial Hospital. She had become pregnant five months before admission and was now sent to the hospital because of severe intra-abdominal pain. The pains were centered about the left upper quadrant and left lumbar area, and were unrelieved by $\frac{1}{2}$ grain of morphine. There were no uterine contractions or vaginal bleeding. Intravenous pyelography and urine examination were essentially negative. The abdomen was markedly distended, rigid, and a soft tender mass of doughy consistency could be palpated in the upper left quadrant of the abdomen. Blood examination: Hb. 84 per cent, R.B.C. $4\frac{1}{2}$ million, W.B.C. 17,000, Poly. 78 per cent. Temperature was 100.8° F., pulse 84. A diagnosis of twisted ovarian cyst was made and operation advised. On opening the abdominal cavity, free straw-colored fluid escaped and the uterus was seen to be the size of five months' pregnancy. A mass, the size of a grapefruit, consisting of left tube and ovary was found in the upper left quadrant. Examination of this mass proved it to be a twisted ovarian cyst and a Fallopian tube with evidence of necrosis and gangrene in both the tube and cyst wall. The gangrenous and twisted ovarian cyst and the gangrenous tube were removed. During the entire operation, the uterus was carefully avoided.

The laboratory reported a cyst measuring ten centimeters in diameter with hemorrhage, infarction and destruction of all normal ovarian tissue. Pathologic diagnosis was torsion of pedicle with infarction and hemorrhage.

The postoperative course of the patient was uneventful, no uterine contractions were felt. No vaginal bleeding was noted and to all intents, the pregnancy continued without the presence of either ovary. Before discharge from the hospital, the patient experienced the sensations of fetal movements and on the thirteenth postoperative day, she was discharged with the pregnancy intact.

For purely empiric reasons, synthetic progesterone (proluton, by injection or pranone, oral) was administered to the patient the day following the operation.¹ Ten milligrams by hypodermic daily for twelve days, and thirty milligrams orally were given daily for the next week and then 10 mg. until the seventh month. On May 25, 1943, exactly four months after operation, she was delivered by Dr. Warner of a six pound, four ounce normal male child. It was a spontaneous delivery and normal post partum.

Discussion

Owing to the acuteness of her complaints, despite the presence of a five months' pregnancy, laparotomy had to be resorted to. The necrotic and hemorrhagic condition of the remaining ovary left no choice as to the procedure—i.e., salpingo-oophorectomy. The questions of course at the time were whether operative manipulation (although uterus was not handled) and peritoneal irritation would induce uterine contractions and whether the pregnancy would continue. When the complete destruction of the only remaining gonad was disclosed, it was felt that the continuation of the pregnancy and its maintenance was already under control of the placental hormones, since it is generally accepted that with the beginning of the third month of gestation, the placenta produces increasingly large amounts of corpus luteum hormones while the production of corpus luteum hormones by the ovary rapidly di-

minishes. The administration of additional progesterone may have helped to maintain the pregnancy, but most likely the gestation would have continued even if the luteal hormones had not been administered.

The interesting point of the case is the fact that conservative surgery permitted this woman to have a second child even though at the time of giving birth, the patient possessed no ovaries. The fact that both ovaries had been totally extirpated is shown by the complete amenorrhea since the delivery (now ten months) and the manifestations of early menopause.

Summary

A report of a successful full-term pregnancy in a patient possessing only one ovary which had to be removed after five months of gestation is presented. The case adds evidence to the belief that neither one nor both gonads nor the corpus luteum are necessary for the continuation of pregnancy once the placental hormones are elaborated in sufficient concentration.

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PREVENTION OF POSTOPERATIVE DISTENTION

THOMAS J. PARKS, M.D., NEW YORK, N. Y.

POSTOPERATIVE distention is a troublesome symptom that often disturbs the surgeon and patient during the first few days after celiotomy. The purpose of this report is to suggest a simple procedure which has been found to prevent its occurrence in most instances of lower abdominal surgery. This procedure is to express manually, as nearly as possible, all the air from the abdominal cavity immediately prior to closing the parietal peritoneum.

The rationale of this supposition is that the abdominal cavity is ordinarily nonexistent or empty except for a few ounces of thin fluid and that air is forced into it by atmospheric pressure. This air must cause discomfort as is demonstrated when air is forced into the abdominal cavity in testing the patency of the Fallopian tubes (Rubin test). The amount of discomfort seems to be in proportion to the amount of gas used. Also, it was observed that patients who were delivered by extraperitoneal cesarean section often had no distention or gas pains. This is in contrast to the not uncommon occurrence of distention following the ordinary transperitoneal section. No air gets into the abdominal cavity when the extraperitoneal operation is successfully performed, as the peritoneal cavity is not entered.

In studying the general subject of pneumoperitoneum, it was found that several years ago it was used as an aid in the diagnosis of intrauterine conditions with x-ray.¹⁻³ It was very soon observed that by substituting carbon dioxide for oxygen or air, the untoward symptoms were diminished. Also, the patient experienced much less discomfort when a small amount of gas was used in comparison to a larger quantity. Massive inflation of the abdomen sometimes resulted in marked distress or collapse of the patient.⁴

No attempt is made to control the air that gets into the abdominal cavity during peritoneoscopic examination, however, before withdrawing the instrument the air is encouraged to escape and sometimes pressure is made upon the abdomen to assist the evacuation.⁵

Deflation, by expressing the air from the abdominal cavity immediately prior to closing the peritoneum, was therefore tried clinically and gave almost uniformly good results which prompted this communication.

It should be emphasized that this procedure is not advocated as a preventive of ileus due to mechanical obstruction or infection. Also, it cannot be expected to have any effect on distention within the bowel or to overcome the untoward aftermath of rough handling or traumatism.

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Department of Reviews and Abstracts

Selected Abstracts

Labor Complications

Kassebohm, F. A., and Schreiber, M. J.: Myometrial Mobilization, *Am. J. Surg.* 62: 65, 1943.

Modern tendencies in obstetrics are toward the shortening of labor and delivery. Already procedures to reduce the length of the second and third stages of labor are in common use. The authors now attempt to reduce the first stage of labor by utilizing rupture of the membranes in conjunction with pituitrin or thymophysin. They believe that the dangers associated with the use of pituitrin have been markedly exaggerated, and that "it has been blamed for much and is guilty of little."

In patients seen early in labor, or in whom labor was induced with pituitrin was used, and for those seen after the onset of labor and with cervical dilatation at a minimum of 4 to 5 cm., thymophysin. These preparations were given after rupture of the membranes at 20-minute intervals throughout the first stage until full dilatation was achieved at which time delivery was effected. The patients were carefully observed by repeated vaginal examinations. Analgesia was also employed without materially influencing the action of the oxytocics. A total of 565 cases was studied, and the average duration of labor under the above regime was 8 hours. There were no complications or accidents.

Contraindications to the method include unengagement of the presenting part, noneffacement of the cervix, or when the cervix is longer than 1.5 cm., and inadequate knowledge of the pelvic capacity and architecture.

FRANK SPIELMAN

Menopause

Quaranta, A. P.: Involutional or Menopausal Psychosis, *An. Catedra de clin. ginec.* 2: 304-306, 1943.

The influence of endocrine factors in mental illnesses is profound, but not yet thoroughly understood. The author states that, as in puberty, psychic disturbances at the climacteric may be elemental, or true psychoses. The elemental disturbances include change in ideas, character and feelings. The principal symptoms are irritability, mysticism and religious exaltation, eroticism of varying degrees, jealousy and suspicion, and hypochondria. These may be exaggerated in some cases with fixed ideas of fear and doubt, and impulsive phobias and compulsions.

A distinction may be made between a psychosis of any type that may appear at the climacteric and a true climacteric psychosis. The symptoms of the former are likely to be modified by symptoms characteristic of common menopausal emotional and mental aberrations. True climacteric psychosis is an acute condition, which exhibits itself in anxious melancholy or mental confusion in various clinical forms:

simple, delirious, hallucinatory, stuporous. This psychosis does not appear at any time during the menopause, but at a certain time and under the direct influence of a genital disturbance, such as sudden cessation of the cycle, abundant hemorrhage, or pain in the genital organs.

The most common type of psychosis seen at the climacteric is depressive, but there are also paranoid, catatonic and hysterical forms. Involutional psychosis is largely due to the following causes: a cycloid personality which may have been more or less evident; endocrine and humoral factors related to the involutional process; multiple psychogenic influences; and the vascular factor.

The prognosis is generally favorable, especially in the depressive type. Shock treatments and organotherapy have yielded satisfactory results. At times, psychotic manifestations at the menopause mark the beginning of senile or arteriosclerotic dementia.

J. P. GREENHILL

Pineda, R.: Treatment of Surgical Menopause by Implantation of Crystalline Estrogens, An. Catedra de clin. ginec. 2: 156-204, 1943.

This subject is discussed by the author based on a study of 70 cases. Complete hysterectomy had been performed in 22, hysterectomy with unilateral adnexectomy in 16, and hysterectomy alone with preservation of the adnexa in 32.

Twenty-four patients received dipropionate of dioxidiethylstilbene in quantities of 10 to 30 mg. All were free of symptoms at the end of the first month. Twelve patients received diacetate of dioxidiethylstilbene in quantities of 10 to 20 mg. Improvement was somewhat slower but was evident in all cases by the end of a month. The nine patients who received dioxidiethylstilbene showed immediate and rapid improvement, which was attributed to the small size of the crystals, which apparently resulted in more rapid absorption. All patients in this group were free of symptoms during the second week. Estradiol dipropionate was used in 23 cases. Improvement was rapid and consistent, being complete in all cases after the third week. Dipropionate of dihydrofolliculin was used in two patients whose ovaries and tubes were preserved. Symptomatic improvement was marked after the fourth week.

Disturbances observed after implantation were of two types, local and general. Although severe symptoms of nausea, vomiting, headache, vertigo, etc., often accompany estrogen treatment orally or parenterally, these were lacking in the patients receiving implantations of crystals. It was not necessary to remove the crystals in a single instance, and the few patients who had slight symptoms generally improved within three days, and always within the first week.

There was a marked influence in many of these patients on secondary sexual characteristics. The vulva and vagina changed their appearance from that of senile atrophy to increased size and color that was distinctly noticeable. Libido returned in many patients, and some also had reappearance of the orgasm; twenty-seven patients were thus affected. There was increase in size and change in color of the breasts and mastalgia was present in a few cases. The clinical observations were controlled by vaginal smears and biopsies.

The author concludes that implantation of estrogenic crystals yields effective and lasting results. Complications and intolerance are practically nonexistent. If feasible, crystals of natural hormone should be used; it is more economical, with results as lasting or more so, and with practically no secondary effects. The effect on the symptoms of the menopause is immediate. Reappearance of libido is a fact worthy of being considered for its effectiveness. Vaginal smears reflect clearly the progress of estrogenic treatment. Optimal dosage to produce an effect lasting more than six months is about 20 mg.

J. P. GREENHILL

Alvarez, C., Geary, E., and Belizan, L.: Basal Metabolism in the Menopause, *An. Catedra de clin. ginec.* 2: 224-230, 1943.

The authors studied the basal rate in a group of 40 selected cases. Clinical and gynecologic investigations were carried out, as well as metabolism tests. The patients all had a natural menopause, and all the patients had menopausal symptoms severe enough to cause them to seek medical attention. It was thought that if the climacteric has an influence on basal metabolism, it would be most apparent in the group with symptoms. The symptoms for which the patients sought relief were the usual ones: dyspnea, palpitation, hypertension, headache, neuralgia, increased weight, psychic disturbances, etc.

Nine of the 40 patients had metabolic rates of more than plus 10; five, of less than minus 10; and 26 had normal rates, i.e., between minus 10 and plus 10. Clinical analysis of the nine patients with high metabolic rates showed that except for one patient with definite hyperthyroidism, all the others had hypertension, which is known to be accompanied frequently with increased basal metabolism. Only one of the patients with a low metabolic rate had an exceedingly low rate, and her menopausal symptoms did not differ from those of patients with normal rates.

An additional statistical study was made to determine the incidence of hyperthyroidism in different age groups of women. In a series of 193 cases, the incidence in patients 46 to 50 was higher than in those from 41 to 45, but not so high as in any of the groups representing five-year age periods from 21 to 40.

The authors conclude that their evidence indicates that alterations in the basal metabolism are not directly attributable to the menopause, but rather to disturbances and diseases that are coincidental.

J. P. GREENHILL

Kurzrok, L., and Rothbart, H.: Treatment of Female Menopause With Methyl Testosterone and Stilbestrol, *Am. J. Surg.* 56: 636, 1942.

The authors treated 16 menopause cases both natural and surgical with methyl testosterone and stilbestrol, administered orally. In addition to the flushes, headaches, and sweats present, 3 of the patients complained of arthralgias, and 3 of pruritus vulvae. Dosage of the preparations varied; from 5 to 25 mg. of methyl testosterone was administered daily together with 2 to 3 mg. of stilbestrol. The duration of treatment was from 1 to 6 months. Improvement or complete relief of the menopause symptoms was obtained in all cases. Two of the 3 patients complaining of pruritus vulvae were relieved and 1 was unimproved. The 3 cases of arthralgia were improved in varying degrees. One patient showed transient lowering of the voice during therapy. No other evidence of masculinization was noted.

FRANK SPIELMAN

Menstruation

Mackey, R.: Anovulatory Menstruation, *M. J. Australia* 1: 505, 1943.

The theories of anovulatory menstruation are reviewed. The author goes into detail in his description of the pathologic picture of the premenstrual or secretory endometrium, the presence of which is essential for the diagnosis of ovulation. The anovulatory endometrium has its own characteristic pathologic picture.

Clinically, anovulatory cycles occur at either end of the menstrual history of woman. The irregularity of the cycles at the menarche and menopause may be an indication of early and late anovular phases. The author stresses the fact that the diagnosis of anovulation cannot be made on result of one biopsy. Treatment has not

been satisfactory. The primary failure appears to be in the functional control of the anterior pituitary in ripening the follicle and causing it to rupture. Other means of treatment with hormones and x-ray have not produced the desired result.

WILLIAM BERMAN

Solomons, Edward, and Widdess, J. D. H.: *The Action of Certain Antispasmodics on Uterine Muscle*, Irish J. M. Sc. 216: 637, 1943.

A preliminary report is given of the effect of trasentin, penthidine hydrochlorida, and syntropan on constrictions of the human uterus. The usual rubber bag technique was used to record constrictions.

Twenty-one human patients were observed of whom 9 were suffering from dysmenorrhea. Of 13 patients treated with trasentin, 10 showed no effect, and 3 showed relaxation. Six patients were treated with penthidine. One showed relaxation, and 5 showed increased activity of the uterine muscle. Syntropan was used in only 2 cases, both of which showed relaxation.

L. M. HELLMAN

Quaranta, A. P.: *Puberal Psychosis*, An. Catedra de clin. ginec. 2: 298-303, 1943.

The various types of psychopathies that appear at puberty, and sometimes continue, with reappearance of symptoms at each menstrual period, require a hyporesistant constitution for their development, according to the author. Factors which contribute to this are heredity, consanguinity, alcoholism in the parents, environmental conditions, emotional shocks, etc. Psychic disturbances in puberty range from simple neuroses to frank psychoses. Among the elemental psychoses are simple depressions with tendencies to solitude and retirement, excessive slowness, or marked timidity in contrast with the patient's previous behavior. On the other hand, some girls display excitation of varying degree, manifesting itself in excessive activity, coquetry, talkativeness, turbulence, insomnia, mischievousness, stubbornness, deceit, religious mania, etc.

When the disturbance is more serious, one observes various hysteric symptoms, neurasthenias, hypochondria related to the new sensations of menstruation, mental anorexia, obsessions, especially relating to insecurity, morals and chastity. In some patients there are certain malignant tendencies: cruelty to animals, compulsion to steal, to set fire to things and even to murder. Some want to see the world, be free, and live adventurous lives.

Pubertal psychoses may take any form, that is, any known psychosis may appear at this period, although its symptoms and development may be modified by the influences attending the patients sexual awakening. In types with delirium, this may be of erotic or religious type. Confusion may be confined to acute hallucinations, experienced chiefly at night. The type of mental confusion usually considered most common in puberty is stuporous, with acute hallucinatory crises.

The prognosis is favorable in the elemental forms, but becomes serious in generalized psychoses as well as in catatonic or hebephrenic forms, because of the tendency to schizophrenia. Improved results depend on conscientious cooperation between gynecologist and psychiatrist. Shock treatments and other modern psychiatric methods have greatly improved the outlook in these cases. In patients with mild psychic disturbances, ultimate mental health is largely dependent on the wisdom and understanding with which they are guided in sexual matters and other emotional expressions at this period.

J. P. GREENHILL.

Rutherford, Robert N.: Physiological Intermenstrual Bleeding—Gross or Microscopic—as a Possible Diagnostic Aid in Abdominal Pain Studies, *West. J. Surg.* 52: 62, 1944.

Intermittent menstrual pain or *Mittelschmerz* was first described in 1847. In 1928, it was first observed that microscopic uterine bleeding may occur periodically between the fifteenth and nineteenth days of the menstrual cycle. This has been found to occur in 75 per cent of Rhesus monkeys at the time of ovulation. Gross bleeding is also occasionally seen in women.

Periodic intermenstrual pain associated with ovulation may be due to rupture of the follicle, chemical irritation of the adjacent tissues by the follicular fluid or related to vascular or nerve response. The author carefully follows 20 normal patients without intermenstrual pain for a period of 1 year. The patients were instructed to inject 1 ounce of saline in the vagina each morning during their estimated ovulation period and collect the washings in a bottle. These daily washings were examined microscopically for blood. When blood was found, a pelvic examination was done and an endometrial biopsy taken. In 237 cycles, microscopic blood was found in 67.9 per cent. It appeared at an average 11.7 days before the onset of the next period. The blood was usually present 3 days. Of the 20 patients studied, 17 showed microscopic bleeding in one or more cycles. On pelvic examination, 79 per cent had a sense of fullness and tenderness, and 18 per cent had definite abdominal tenderness associated with bleeding. Endometrial biopsies taken at the time of bleeding usually showed early secretory phase. There was no definite relationship with libido.

In another series of patients with periodic pain similar findings were noted as in the above group. Many of the patients in this group presented a problem in the differential diagnosis of appendicitis and ovulation pain. It is the author's opinion that the simple technique of vaginal washings with a search for microscopic bleeding will further aid in the differential diagnosis. It may also help in dating ovulation for sterility, or contraceptive study.

WILLIAM BICKERS.

Loeser, Alfred A.: Effect of Emotional Shock on Hormone Release and Endometrial Development, *Lancet* 244: 518, 1943.

The author reports four cases of suppressed menstruation due to shock. In three instances the shock or psychic trauma was due to bomb explosions, and in the other to the omission of the use of contraception.

The specimens obtained by curettage were examined by Professor Emil Novak. It is concluded in summary that "four women who had always menstruated regularly missed a period after an emotional shock. Histological examination of the biopsy specimens showed an endometrium at the stage of development it would normally have reached at the time of the shock, suggesting that the shock caused an immediate arrest of development by interruption of the release of the proper hormones."

FRED L. ADAIR.

Morton, S., Gerson, R., and Biskind, Leonard H.: Nutritional Deficiency in the Etiology of Menorrhagia, Metrorrhagia, Cystic Mastitis, and Premenstrual Tension, *Surg., Gynec. & Obst.* 78: 49, 1944.

Based on two earlier observations, namely, that estrogen is inactivated in the liver, and that this inactivation cannot be accomplished in vitamin B deficient animals, the authors have made observations on 104 patients with menorrhagia, metrorrhagia, cystic mastitis, premenstrual tension, and uterine myomata. Thirty-

nine of these patients were observed primarily because they showed clinical signs of vitamin B deficiency. Of these 37 had one or more of the above-mentioned conditions, and vice versa, 52 patients whose main complaint was thought to be due to excess estrogen, showed signs and symptoms related to vitamin B avitaminosis. Many of these patients had a low level metabolic rate. Administration of thyroid without vitamin B caused an exacerbation of the signs and symptoms B avitaminosis. The particular factor of the B complex responsible for this phenomenon is not known.

L. M. HELLMAN.

Friedmann, Ernst: Prostigmin in the Treatment of the Delayed Period, Brit. M. J. 4330: 11, 1944.

The biochemical reaction of the drug on the parasympathetic control of menstruation is mentioned. The author gave 1 mg. of prostigmin intramuscularly on 3 successive days, this treatment being discontinued after the first or second injection if the menstrual flow was restored. With the exception of two cases that failed to respond, the longest interval between the last injection and the onset of menstruation was 72 hours. The side effects of the drug are described. Favourable results were obtained in 94.5 per cent of the cases of delayed period not due to pregnancy. There is no tendency of the drug to interfere with the course of pregnancy.

WILLIAM BERMAN.

Miscellaneous

Hartman, Carl G.: Regeneration of the Monkey Uterus After Surgical Removal of the Endometrium and Accidental Endometriosis, West. J. Surg. 52: 87, 1944.

At the Carnegie Institute, the technique for the recovery of early ova in the monkey consisted of enucleation of the entire endometrium as an intact sac. Following laparotomy, the uterus was incised longitudinally down to the endometrium and the endometrium was then dissected out with scalpel and scissors. In some experiments the exposed myometrium was then wiped clean with a cotton sponge so that no vestige of the mucosa was visible to the naked eye. These operations were followed by studies of the regenerated endometrium, and it was discovered that complete regeneration often occurs as soon as the sixteenth postoperative day. In some monkeys, castration was performed at the same time that the endometrium was removed, and under the stimulation of estrone pellet implants the regeneration in these animals was equally as rapid. Photomicrographs of regenerating endometrium were shown. The occurrence of normal pregnancies on the regenerated endometrium gives ample evidence that the uterus is able to reconstruct an endometrium which is normal anatomically and functionally.

The conclusion justifies that the regeneration of an almost completely eliminated endometrium proceeds at a very rapid rate.

In the process of removing the endometrium, it is inevitable that bits of tissue are dropped into the peritoneal cavity. Endometriosis and formation of chocolate cysts were common. However, this does not prove or disprove the Sampson theory for 2 reasons: (1) The necrotic, desquamated tissue of menstruation is less likely to transplant than the normal endometrium which was spilled in these experiments. In the experiments of Markee, it was found quite difficult to transplant menstruating endometrium to the anterior chamber of the eye while the other transplanted easily. (2) The uterotubal junction is of such a character as to make it difficult to force any liquid from the uterus to the tubes, especially during menstruation.

WILLIAM BICKERS.

Reynolds, Philip A.: The Clinical Significance of the Rh Factor, *West. J. Surg.* 52: 103, 1944.

Erythroblastosis is the result of Rh antibodies in the blood of an Rh-negative mother carrying an Rh-Positive fetus in her uterus. The Rh-positive fetus results from fertilization by an Rh-positive father. However, such a potentially dangerous mating as an Rh-positive male and an Rh-negative female does not mean that all babies will have erythroblastosis. Indeed, it is known that they do not. The following reasons are given: (1) The titer of Rh antibodies in the mother, particularly in the initial pregnancy, may not rise sufficiently high to produce erythroblastosis in the fetus. (2) The Rh-positive father may be a heterozygote for the Rh factor. (3) Transfer of the fetal red blood cells across the placental site may not occur unless there is trauma from fetal movements, or the development of placental infarcts and in this case no isoimmunization will take place. However, the incidence of erythroblastosis from a mating of an Rh-positive male and an Rh-negative female is sufficiently high so that they should be warned of the potential danger.

Evidence is presented to show that repeated abortions and stillbirths without other apparent causes are most common in this type of mating. In cases of repeated abortions, the Rh factor for both man and wife should always be determined.

Severe anemias of pregnancy and the puerperium may result when an Rh-positive mother carries an Rh-negative fetus. In this case the process is reversed. The fetus produces the Rh antibodies which upon entering the maternal circulation attack the mother's red cells.

Transfusion reactions should be expected in women who have given birth to infants with erythroblastosis and those with a history of repeated abortions if they are transfused with Rh-positive blood. Isoimmunization may also occur after one transfusion so that subsequent transfusions will result in severe or fatal reactions. In transfusing an erythroblastotic infant, Rh-positive and Rh-negative blood should be alternated.

WILLIAM BICKERS.

Hartman, Carl G.: Recovery of Primate Eggs and Embryos, *West. J. Surg.* 52: 41, 1944.

Recovery of primate eggs and embryos for the study of mammalian development has occupied the attention of this author and his colleagues at the Carnegie Institute. A brief history of the Carnegie Institute is presented along with the evolution of knowledge relative to the development of early ova. Progress was accelerated by the ability of the investigator to raise under laboratory conditions, a large colony of Rhesus monkeys.

The author developed a technique by which ovulation in the animal could be diagnosed by rectal palpation. Following ovulation in the monkey, various techniques were employed for recovering the ova. They were obtained by aspiration of the Graafian follicle, by irrigation of the tubes following salpingectomy, by washing free ova from the uterus, by transabdominal insertion of a needle into the uterine cavity, and by irrigating the uterus with Locke's solution collecting the irrigating fluid and contents from the cervix. The most satisfactory early fertilized ova have been obtained by performing a hysterectomy soon after the established time of implantation. The uterus is removed, opened under Locke's solution. Careful histologic sections are made at the site of the chorionic vesicle. It has been shown that implantation in the monkey occurs at the beginning of the tenth day. Hertig and Rock, employing similar techniques in the human being, estimated the implantation time the seventh or eighth day. Implantation in both occurs near the midline of the ventral or dorsal surface of the uterus. The human ovum eats its

way into the decidua until completely covered by epithelium while in the monkey, the ovum remains on the surface.

Ovulation time in relation to the menstrual cycle has been adequately studied in the monkey, chimpanzee and in woman. Observations were made on the basis of rectal palpation in the monkey and study of the embryo in relationship to isolated fertile coitus in the monkey, chimpanzee and woman. The normal spread of ovulation time in the monkey is 8 to 16 days with only a few exceptions occurring on the 17, 18, 19, 29 and 23rd days. Ovulation outside of the normal range was explained on the basis of some organic disease of the ovary, or some extraneous influence which is described in detail for each case of delayed ovulation. The explanation of Rock, et al., suggests that ovulation time in the human being closely parallels that in the monkey. Only 2 per cent of monkeys ovulate outside of the defined fertile period. The functional life span of the corpus luteum in the monkey is subject to some variation while in the chimpanzee the preovulatory interval is more variable. In man, there is apparently a relatively constant postovulatory period usually about 16 days. The full truth of the above statement as regards man is yet lacking.

WILLIAM BICKERS.

Newborn

Bayona, E., and Gori, R. M.: *Fetal Erythroblastosis*, *Obst. y ginec. Latino-Americanas* 1: 359-364, 1943.

The following forms of erythroblastosis are recognized: Hydrops fetalis; icterus gravis of the newborn; congenital anemia; hemorrhagic diathesis; and nonclassifiable forms without edema, anemia, icterus, or hemorrhagic diathesis, observed in the still-born.

When a mother, who is Rh negative, carries a fetus who has inherited the Rh factor from the father, an isoimmunization of the mother is produced. Then the maternal agglutinin (anti Rh), on passing into the placental circulation, causes cellular destruction of the fetal blood and gives rise, according to its intensity, to the various clinical forms of erythroblastosis. The Rh factor, like the A and B factors of blood groups, is considered as a dominant mendelian character transmitted by a pair of genes Rh rh; the incidence of the genotype Rh Rh is 37 per cent; of Rh rh 47.6 per cent and of rh rh 15.4 per cent.

A few cases have been observed in which the Rh factor could not be demonstrated, and the authors suggest that in these, the older theory of heterospecificity of the mother should be considered. This is fundamentally similar to the theory of isoimmunization, and postulates that a mother of group O who carries a fetus of group A or B would produce agglutinins against A or B, capable of acting on the fetal blood.

Burnham believes that a maternal deficiency—even subclinical—of vitamin C may be a factor in the development of erythroblastosis.

In view of the probable cause of erythroblastosis, the diagnosis depends on studies before and after parturition. Before, the mother may present signs and symptoms which may lead to suspicion of erythroblastosis in the fetus. These include multiparity, mother Rh negative and father Rh positive; yellowish amniotic fluid, increased icterus index, erythroblastosis in previous offspring, toxemia, intrauterine death of the fetus, systolic murmur of the intrauterine fetus, etc. Radiologically, a cephalic halo can be observed in instances of hydrops fetalis, and in some instances, the fetus is in the position of Buddha, due to edema. After birth, the various types of erythroblastosis must be differentiated from physiologic icterus, hemorrhagic diseases of the newborn, congenital heart disease, congenital syphilis, absence of biliary ducts, familial acholuric icterus, Winckel's disease and hypoproteinemia.

Blood studies are of prime importance in diagnosis, including blood group, cross-match, chemical determinations, especially of protein and uric acid, vitamins, Rh factor, etc. At autopsy, it is important to investigate deposits of hemosiderin in the fetal organs. Microscopically, there is a marked increase in osseous density in all or part of the diaphysis, and zones of rarefaction.

From the therapeutic standpoint, recognition of erythroblastosis is extremely important, in avoiding possibility of dangerous reactions from transfusion in the mother. In any suspected case, vitamin C should be administered in large doses. Interruption of the pregnancy or cesarean section should be done only with specific maternal indications. In suspected cases, analgesia and anesthesia should not be used.

Treatment of the newborn infant should be with repeated transfusions (60 c.c.) never with maternal blood. Vitamin K should be given in doses of 2 to 4 mg. Mortality and serious sequelae are reduced by these means, but unfortunately some of the children who survive have secondary manifestations, such as juvenile cirrhosis, spastic dysplasia and mental deficiency.

J. P. GREENHILL.

Torrey, John C., and Reese, Martha K.: Initial Aerobic Flora of Newborn (Pre-Mature) Infants' Nature, Source and Relation to Ultraviolet Irradiation and Face Masks, Am. J. Dis. Child. 67: 89, 1944.

This study was based on over 150 infants born in the obstetric division of New York Hospital, and were admitted, generally within one or two hours, to the unit for premature infants in the pediatric division.

Cultures were made from the throats and nasopharynges on the first, second, third and fourth days of life, and subsequently at irregular intervals until discharged, which usually occurred in three to four weeks.

The authors concluded that the initial aerobic bacterial flora of the throat and nasopharynx of artificially fed newborn infants is largely acquired through direct contact with adults and not from the parturient canal. The principal vehicle of transfer is droplets of saliva. However, on one occasion, the gonococci were found in the infants' throats and also in the maternal birth canal. Up to 16 hours after birth, the nasopharynges and throats of about 80 per cent of 16 infants exhibited sterility with the cultural methods employed.

Ultraviolet irradiation did not retard the acquisition from hemolytic streptococci, but did delay infection with the hemolytic strains of *Staphylococcus aureus*. Between twenty-four and forty-eight hours after birth 50 per cent of 12 infants in wards exposed to ultraviolet irradiation still showed sterility, as contrasted with 12 per cent of 16 infants in wards not so exposed. The strains of streptococci and of *Staphylococcus aureus* normally present in the throats and nasal passages of adults passed to some extent through the types of face masks worn, even in the absence of coughing or sneezing. The acquisition of hemolytic strains of *Staphylococcus aureus* was highest in the late winter and spring months and lowest in the early fall.

JAMES P. MARR.

Pregnancy, Complications

Bonilla, J. Lopez: Tuberculosis and Pregnancy, An. Catedra de clin. ginec. 2: 307-314, 1943.

During the course of medical history, medical opinion has varied widely as to the influence of pregnancy on pulmonary tuberculosis. Attempts have been made to determine clinical forms of tuberculosis that react unfavorably to pregnancy, but no definite conclusions have emerged. Hence, it is impossible to systematize the

prognosis in the tuberculous pregnant woman according to the clinical type of tuberculosis, and pregnancy does not impart any special character to the evolution of tuberculosis. A review of the most careful statistical studies, and the author's own experience leads to the opinion that there is no appreciable difference in the results of treatment for tuberculosis, whether the patient is pregnant or not. Pregnancy per se, does not exert a deleterious effect on tuberculosis, but the ultimate outcome of the disease is determined by its type and extension, and the circumstances of the individual pregnancy.

Within the first three months of pregnancy, there is one clear and definite indication for induced abortion. This is in tuberculosis which is recognized for the first time during pregnancy, with a progression that indicates it would be considered amenable to collapse therapy, but in which, because of local or general conditions, it is not possible to apply it. With this criterion, one eliminates as an indication for abortion benign types of tuberculosis whose possible exacerbation should yield to hygienic treatment and the serious types, in which collapse therapy cannot be used, and whose outlook is equally dark, with or without pregnancy.

Following this policy, the author found that abortion was necessary in only one of 18 cases in which the tuberculosis appeared with pregnancy and the patients were examined within the first three months. The patient in the exceptional instance was a primipara, aged 25, with fibrocaceous tuberculosis of the upper third of both lungs, in whom pneumothorax could not be carried out on either side. In the others, pneumothorax or phrenicectomy was performed, and the tuberculosis was controlled so that the patients were in excellent condition when they arrived at term.

J. P. GREENHILL.

Leon, J., and Lascaro, Gonzales, J. M.: *Fibroma of the Ovary in a Pregnant Woman*, Arch. clin. obst. y ginec. "Eliseo Cantón" 2: 287, 1943.

The authors report the case of a multipara aged 28 years, from whom a solid tumor of the ovary was removed in the third month of pregnancy. This tumor was the size of an orange and its pedicle was twisted. On its periphery was the corpus luteum of pregnancy. The tumor proved to be a fibroma. Gestation continued to term. The authors review the literature concerning solid tumors which have complicated pregnancy.

J. P. GREENHILL.

Erratum

In the article by Commander Phineas Bernstein, M.C., USNR, entitled "Hysterosalpingography, a Routine Aid in Gynecological Diagnosis" appearing in the August issue, page 189, the following corrections should be made in the illustrations and script:

Illustrations

- Fig. 3 Correct title now appears under Fig. 4.
- Fig. 4 Correct title now appears under Fig. 5.
- Fig. 5 Correct title now appears under Fig. 6.
- Fig. 6 Correct title now appears under Fig. 8.
- Fig. 8 Correct title now appears under Fig. 3.

Script

- Fig. 3 p. 192 should be omitted.
- Fig. 4 p. 192 should be Fig. 3.
- Fig. 5 p. 194 should be Fig. 4.
- Fig. 8 p. 196 should be Fig. 6.
- Fig. 3 p. 197 should be Fig. 8.
- Fig. 6 p. 197 should be Fig. 5.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MARCH 14, 1944

The following papers were presented:

- Late Recurrence in Carcinoma of Fundus Uteri.** David N. Barrows, M.D. (For original article, see page 422.)
A Consideration of Therapeutic Abortion. Samuel A. Cosgrove, M.D. (For original article, see page 299.)
-

THE CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF FEBRUARY 18, 1944

The following papers were presented:

- Androgenic Therapy in Malignancies of the Female Genitalia: Preliminary Report.** Stuart Abel, M.D.
Carcinoma of the Cervix and Pregnancy: A Study of Eight Cases. Alfred J. Kobak, M.D., J. E. Fitzgerald, M.D., Vincent C. Freda, M.D. (by invitation), and Louis Rudolph, M.D.

MEETING OF MARCH 17, 1944

The following paper was presented:

- Irregular Shedding of the Endometrium, a Specific Cause of Menorrhagia.** John L. McKelvey, M.D. (by invitation).

MEETING OF APRIL 21, 1944

The following papers were presented:

- A Study of Maternal Morbidity.** William G. Cummings, M.D.
Statistical Analysis on Cesarean Sections at the Chicago Lying-in Hospital. Eugene G. Free, M.D. (by invitation), and William J. Dieckmann, M.D.

MEETING OF MAY 19, 1944

The following papers were presented:

- Internal Endometriosis.** Harold O. Jones, M.D.
Pathology of Endometriosis. George H. Gardner, M.D.
Diagnosis of Endometriosis. Eugene A. Edwards, M.D.
Treatment of Endometriosis. Edward Allen, M.D.

Item

American Board of Obstetrics and Gynecology, Inc.

The annual meeting of the Board was held at Pittsburgh, Pennsylvania from June 7 to June 13, 1944, at which time ninety-five candidates were certified.

A number of changes in Board regulations and requirements were put into effect designed to aid both civilian as well as candidates in the Service. Among these is the waiver, temporarily, of our A.M.A. requirement for men in the Army or Navy, especially for those who proceeded directly or almost so from hospital services into Army or Navy Service, upon a statement of intention to join promptly upon return to civilian practice. At this meeting the Board also has accepted a period of nine months as an academic year in satisfying our requirement for certain years of training. This is only for the duration and even men who are not eligible for Military Service but who are nevertheless in hospitals where the accelerated program is in effect have been allowed to submit to us this short-time period of training in lieu of our previous requirements.

Beginning with the next written examination, which is scheduled to be held the first Saturday afternoon in February, 1945, this Board will limit the written examination to a maximum period of three hours and in submitting case records at this time, all candidates' case abstracts, whose obstetric reports do not include measurements either by calipers and, as indicated, by acceptable x-ray pelvimetry, will be considered incomplete. Prospective applicants or candidates in Military Service are urged to obtain from the Office of the Secretary, a copy of the "Record of Professional Assignments for Prospective Applicants for Certification by Specialty Boards" which will be supplied upon request. This record was compiled by the Advisory Board for Medical Specialties and is approved by the Offices of the Surgeons-General, having been recommended to the Services in a circular letter, No. 76, from the War Department Army Service Forces, and referred to as the Medical Officer's Service Record. These will enable prospective applicants and candidates to keep an accurate record of work done while in Military Service and should be submitted with the candidate's application, so that the Credentials Committee may have this information available in reviewing the application.

Applications and BULLETINS of detailed information regarding the Board requirements will be sent upon request to the Secretary's Office, 1015 Highland Building, Pittsburgh 6, Pennsylvania. Applications must be in the Office of the Secretary by November 15, 1944, ninety days in advance of the examination date. The time and place of the Spring 1945 (Part II) examination will be announced later.

PAUL TITUS, M.D.

1015 HIGHLAND BUILDING,
PITTSBURGH 6, PA.

American Journal of Obstetrics and Gynecology

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Original Communications

THE TREATMENT OF CARCINOMA OF THE CERVIX DURING PREGNANCY

HOWARD W. JONES, JR., M.D., AND WILLIAM NEILL, JR., M.D.,
BALTIMORE, MD.

(From the Kelly Clinic)

THE treatment of carcinoma of the cervix occurring during pregnancy is complicated by the conflicting facts that radium irradiation is the most trustworthy method of therapy for carcinoma of the cervix, but can damage the developing fetus, especially when used in the early months of gestation. Because of this danger to the child, many observers have concluded that irradiation in any form or dosage is contraindicated, so long as the pregnancy is allowed to continue. Leopold Goldstein and Douglas Murphy¹ in a series of papers in 1928 and 1929 brought together the existing literature, which clearly demonstrated that therapeutic pelvic irradiation during pregnancy is extremely likely to injure the growing fetus and that such injury may result in the birth of a seriously defective child; in 75 instances of irradiation during pregnancy, there was an uncorrected figure of 50.7 per cent defective children. However, a closer analysis of the data reveals extenuating circumstances in many cases; for example, in some instances substantial high voltage roentgen dosage was delivered to a pregnant uterus in the mistaken belief that it was a myoma. This fact, along with our own and the varying experiences of others with cervical cancer, has led us to believe that the conclusion of Goldstein and Murphy, while indicating the danger of irradiation during pregnancy, does not necessarily outweigh its advantage in treating carcinoma of the cervix.

Contributors to the literature have resolved themselves into two principle groups—those who do not permit irradiation of cervix cancer if pregnancy is allowed to continue, and those who feel that properly applied radium irradiation is justifiable and safe. Either point of view

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

is often supported by a single case report issued almost before the patient leaves the hospital so that an estimation of the five-year salvage, or the ultimate outcome for the baby is impossible. There are well over 200 references to this subject in the *Quarterly Cumulative Index Medicus*, but scarcely more than a dozen reports that fulfill the essential requirement of an elapsed time of five years so necessary in a discussion of carcinoma. Thus, many reports are invalid in a discussion of the results of treatment in carcinoma of the cervix, and are also worthless from the standpoint of prognosis for the infant, as it is well known that one of the most serious deformities caused by irradiation, microcephaly, is often not recognizable at birth. A period of about three years must elapse before one can be sure that this distressing condition does not exist.

Our own experience with carcinoma of the cervix during pregnancy, and a study of the reported cases, in so far as they are helpful, has led us to believe that the treatment of such patients must be individualized; one general rule of therapy, which either allows radiation and continuation of pregnancy, or dictates interruption of the pregnancy as a necessary part of the treatment is not applicable. If there is a probability of obtaining a normal child in treated cases, and if the circumstances of the case so justify it, the attending physician must indicate this possibility to the patient. In a multipara with adequate family, it would be unwise to assume even a slight hazard of fetal injury, provided interruption of the pregnancy will not endanger the prognosis for the mother. Many patients pregnant for the first time would desire to entertain a reasonable risk of an abnormal baby, if their own chance of cure was not compromised.

Our problem therefore, is to estimate the risk of an abnormal fetus following irradiation for carcinoma of the cervix during pregnancy, and to examine the prognosis for the mother with and without interruption.

The Risk of Fetal Abnormality Following Radium Irradiation for Carcinoma of the Cervix

In order to estimate the risk of fetal damage with radium in the treatment of cervix cancer during pregnancy, we have collected all cases of this condition and added our own experience. This material is summarized in Tables I and II. Some of the cases herein reported were previously described by Neill² but are included with additional follow-up notes.

There are 48 cases, exclusive of our own, in which irradiation was used sometime following conception and prior to delivery.

One may arbitrarily set three years as the time which must elapse in order to be sure about the occurrence of microcephaly. There are reported only seven normal children which fulfill these requirements.

There are 28 indeterminate cases, that is, cases reported prior to three years after delivery. Practically all of these children are quoted as normal.

There are five examples of abnormal offspring. Two of these five treated many years ago, received x-ray therapy and therefore should be excluded. Two are macerated fetuses. One of these two was irradiated at 4 months and the other at 3; both went almost to term. There remains but a single reported case prior to our own of a living child with microcephaly following radium treatment for carcinoma of the cervix. This patient was treated at 6 months, and both patient and child were living 11 years at the time of the report.

There are also eight reported cases of neonatal deaths due to incidental causes such as measles, pyloric obstruction and pneumonia.

Our own material (Table II and Case Reports) includes 8 instances of prenatal irradiation. There are five children living and normal from three to fifteen years of age. There are two instances of microcephaly, but one of these contracted tuberculosis and died at the age of four years. There is one child who seemed normal in every way, but who died of measles at the age of 18 months.

Combining our own material and the literature, there are twelve children irradiated prenatally who are living and normal more than three years of age. There are 28 children living and apparently normal but reported before three years. There are nine children who died of some unrelated disease before three years. There are three cases of microcephaly.

It is difficult, due to limitation of numbers, to express the risk of microcephaly percentage-wise. If only determinate cases are considered, there are three seriously abnormal children in a total of 15 live births, or 20 per cent. If the entire group is considered, the figure would be three in fifty-two, or 6 per cent.

Five months is sometimes cited as the earliest time at which irradiation should be applied. At that time the fetus is higher in the abdomen, thus affording greater distance from the source of irradiation. There is also said to be less likelihood of abortion, if ovarian function be destroyed at that time. There is little real evidence to support such view although it may well be correct. Of the 48 reported cases, 8 were treated prior to five months. Two of these went to term and delivered macerated fetuses. One is living and well at eight years. Five are said to be living and well, but under three years of age. There are 40 reported cases treated later than 5 months. These yielded 6 children living and normal more than 3 years after delivery, 23 living and normal but reported prior to 3 years of age, 8 children dead of undetermined causes and 3 abnormal children. Two of these last three were treated with high voltage roentgen therapy and can be eliminated for our purposes; the third one treated at 6 months is a living microcephalic 11 years of age at time of report.

Three of our cases were treated prior to 5 months. Two of these were microcephalic, one of which is still living at 3½ years of age. Five were treated after 5 months, and none of these developed microcephaly.

TABLE I

| AUTHOR | AGE | DURATION OF PREGNANCY | CLINICAL STAGE | IRRADIATION | DELIVERY | END RESULT MOTHER | END RESULT CHILD |
|---|-----|-----------------------|----------------|--|---------------------------------------|--|---|
| Mundell ³ | 33 | 25 weeks | I | 1,800 mg. h. each week for 3 weeks 6/12/38 | Cesarean section 9/15/38 | Living under five years 4/18/39 | Living and normal 4/18/39 |
| Herold, K. ⁴ | (?) | 5 months | | Radium | Spontaneous | | Normal |
| Hoffmann, H. ⁵ | (?) | 5 months | | Radium | Spontaneous | | Normal |
| Pouey, ⁶ | 34 | 6½ months | II | 11/28/23—43.2 mc. d. in 8 days | Spontaneous 20 hours labor | Living under five years 5/1/27 | Living and normal 5/1/27, more than 3 years |
| Convelaire, ⁷ | (?) | 5 months | | Radium | Cesarean section 8½ months | | Normal |
| Condamine, R. ⁷ | 38 | 5 months | | Radium | Spontaneous | | Normal |
| Titus, ³ | (?) | 5 months | | Radium | Spontaneous | | Normal |
| Brouha, M., and Gosselin, O. ⁸ | 31 | 7 months | I | 48 mc. d. in 10 days 1800 x 4 post-partum | Cesarean section plus panhysterectomy | Died 18 months, recurrence in broad ligament | Pyloric stenosis. Died from operation |
| Berkley, C. ⁹ | 34 | 26 weeks | I or II | 3,600 mg. h. | Cesarean section plus Wertheim | Living and well 20 years | Living and normal 20 years |
| Van Rooy, A. W. ¹⁰ | 41 | 4 months | I | 4,200 mg. h. 6/9/33 | Spontaneous 1/10/34 | Well under 5 years | Well under 3 years |
| Paroli, G. ¹¹ | 29 | 3 months | | Radium | | | Living and normal |
| Zimmerman, R. ¹² | 33 | 5 months | | Radium | | | Living and normal |

| Amico-Roxas, S. ¹³ | 27 | 6 months | Radium | Cesarean section and hysterectomy | |
|---|-----|---------------|---------------------------------|--|------------------------------|
| Fagioli, M. ¹⁴ | 28 | 6 months | Radium | Cesarean section | |
| Smith, F. R. ¹⁵ | 36 | 6½ months | "Early" Radium | Cesarean section 8 months | Died 18 months |
| Petenyi, G. ¹⁶ | (?) | 5 to 7 months | X-ray | Spontaneous | Died 3 days; atelectasis |
| Gol, F. ¹⁷ | (?) | | X-ray | Spontaneous | Microcephaly and eye damage |
| Goldstein, L., and Murphy, D. P. ¹ | 29 | 6 months | 185 mg. for 24 hours, May, 1916 | Spontaneous 6/21/16 | Microcephaly 11 years |
| Schilling, N. ¹⁸ | 32 | "Advanced" | I 100 mg. for 24 hours | Cesarean section 3/23/23 | Died 3 hours |
| Strauss, A. ¹⁹ | 38 | 5 months | "Operable" | Cesarean section plus panhysterectomy | Died soon after delivery |
| Metzger and Leguen ²⁰ | 31 | 3 months | I 18 mc. d. | Forceps | Died of recurrence 18 months |
| Hartman, H., and Farber, S. ²¹ | 35 | 4 months | II 32.9 mc. d. | Cesarean section and supravaginal hysterectomy | Living and normal 2 months |
| Roy, ²² | 29 | 4 months | 47 mc. d. in 5 months | Spontaneous | Living and normal 2 months |
| Condamine, R. ²³ | 25 | 1½ months | Radium | Spontaneous | Died 10 days |
| | | | | | Died from difficult delivery |

TABLE I—CONT'D

| AUTHOR | AGE | DURATION OF PREGNANCY | CLINICAL STAGE | IRRADIATION | DELIVERY | END RESULT MOTHER | END RESULT CHILD |
|--|-----|-----------------------|----------------|--|---|---------------------------|-------------------------------------|
| McGlinn, J. A. ²⁴ | 31 | 3 months | | 24 mc. d. | Spontaneous | Died 9 months | Macerated at birth |
| Heuze. ²⁵ | 39 | 4 months | | 40 mc. d. | Cesarean section | Living and well 6 years | Living and normal 6 years |
| Karg, C. ²⁶ | 30 | 6 months | "Early," | 55 mg. for 24 hours | Spontaneous | Died 1 year | Living and normal 8 years |
| Bottaro, and Mengoa, ⁸ | (?) | 16 months | | 50 mg. for 24 hours repeated 5 times in 8 days | Cesarean section at term | | |
| Field, C. E. ²⁷ | 39 | 6 months | II | 7,230 mg. h. March 3 to 26, 1919 | Spontaneous 4/26/19 | Died 6/17/20 | Living and well 3 years |
| Pailey, H., and Baggs, H. J. ²⁸ | 35 | 6½ months | | 3,613 mg. h. | Cesarean section at term 4/3/20 | Died of eclampsia 4/16/20 | Normal; died of pneumonia 2½ months |
| Cathala and Mérat ²⁹ | 35 | 7 months | | Radium | Cesarean section and hysterectomy 3 days after radium treatment | Died postoperative | Living under 3 years |
| Garipey, R. ³⁰ | 42 | 7 months | | 100 mg. for 72 hours | Spontaneous | Living and well 10 months | Living and normal 10 months |
| Karg, C. ²⁶ | 33 | 8 months | | 55 mg. for 24 hours | Spontaneous | Living and well 1 year | Living and normal 1 year |
| Heurotey and Chevala ³¹ | 35 | 8 months | | 68 mc. d. 15 days | Cesarean section and hysterectomy at term | Living | Living |

| Porte and deNabias ³² | 36 | 5½ months | 32 mc. d. | Cesarean section 8½ months | Living and well 1 year | Living and normal 1 year |
|---|-----|-----------|----------------------------|---|-----------------------------|------------------------------|
| Hauch, E. ³³ | 36 | 9 months | Radium | Cesarean section and hysterectomy | Died 4 days post-operative | Living and normal |
| Godlewski, E. ³⁴ | (?) | 7 months | Radium | Cesarean section and hysterectomy 8 months | Died with metastases | Living |
| Roy ²² | 28 | 7 months | 27.5 mc. d. 5 days | Cesarean section and hysterectomy | | Normal |
| Roy ²² | 36 | 7 months | Radium | Cesarean section at term | Died | Normal |
| Condamine, R., Voron and Molin ²³ | 38 | 5 months | 25 mc. d. | Spontaneous | Living and well 3 months | Died 1 month |
| Infantizzis | (?) | 7 months | Radium | Spontaneous | | Living |
| Belle ³⁸ | 38 | 5 months | 40 mc. d. | Spontaneous | Died 1 year | Living and normal |
| Döderlein, A. ³⁵ | 33 | 7 months | 2,440 mg. h. | Spontaneous | Died 2 years | Living and normal 2 years |
| Döderlein, A. ³⁵ | 30 | 7 months | Extensive 2,440 mg. h. x 3 | Spontaneous | Died 1 year | Living and normal 9 years |
| Kirtz, L. P., and Pareira, M. D. ³⁶ | 32 | 7 months | I 3,350 mg. h. | Cesarean section | Living under 5 years | Living and normal 3 years |

Our own material more than the literature tends to support the opinion that irradiation is much safer for the fetus, if used after 5 months. We are, therefore, greatly influenced by the duration of gestation in recommending treatment.

At times abortion occurs from 1 to 60 days following the application of radium to the cervix, and there are about 15 such cases reported: about half of these were treated before the pregnancy had progressed five months. It is likely that many more such cases have never been reported. Manipulation of the cervix incident to the treatment could be more responsible for abortion than injury to the child, or destruction of ovarian function.

Dosage of radium is important, but none of the cases with abnormal fetuses received excessive treatment considering the growth. Furthermore, normal children were born to mothers who received as much or higher dosage. It was impossible in our own cases to correlate in any way dosage estimated to be delivered in the region of the child's head with the occurrence of microcephaly.

Risk to the Mother

An estimation of the possible risk which the mother may suffer from the interruption or continuation of the pregnancy is essential in planning treatment. This figure can best be determined by a study of comparable series treated on one hand by irradiation and continuation of pregnancy, and on the other by irradiation with interruption of pregnancy. In discussing the risk to the child, it was pointed out that case reports were issued too soon to be of real value in determining the health of the child; this is likewise true in determining the ultimate outcome for the mother.

In the treated uninterrupted cases (Table I), there are only three mothers living and well more than five years. There are 18 mothers dead, most of these within the first 18 months following treatment. In 24 instances reports of living mothers were issued prior to five years following treatment.

Our own results (Table II) show seven mothers treated during eight pregnancies. Two are dead, one is living at three years, and four mothers treated during five pregnancies are living and well five years or more after treatment.

Unsatisfactory as are these figures, the number of published cases treated with radium plus abortion either spontaneous or induced, is even more meager. Phillipp³⁷ has reported a case living seven years. She was treated at four months and had a spontaneous abortion at 6½ months. Danforth³⁸ reports a case well for seven years in whom a very early pregnancy was curetted from the uterus just prior to inserting the radium. On the other hand, there are at least two reported cases (Moris,³⁹ Danforth³⁸) of instrumental abortion followed by death from infection. Most of the case reports are issued far too soon for an

TABLE II

| NAME | AGE | DURATION OF CLINICAL PREGNANCY | STAGE | TREATMENT | DELIVERY | FOLLOW-UP MOTHER | FOLLOW-UP BABY | POST-PARTUM TREATMENT |
|-----------------|-----|--------------------------------|-------|--|--------------------------------|--------------------------------|--|---|
| O. H.* 17355 | 28 | 6 months | II | 12/18/26 1,762 mc. h. | 1/16/27 Cesarean section | Died met. Sept., 1930 | Living and normal, 3/31/42 | 2/12/30— 500 mc. h. |
| M. B.* 22599 | 32 | 5 months | II | 5/13/30 3,109 mc. h. | 9/12/30 Cesarean section | Living and well, 1942 | Living and normal, 1942 | |
| A. W.* 24792 | 29 | 6 months | I | 11/28/31 2,671 mc. h. 1/ 9/32 843 mc. h. | 2/11/32 Cesarean section | Living and well, 1943 | Living and normal, 1943 | |
| S. B. 30042 | 30 | 7 months | I | 2/23/36 2,940 mc. h. | 6/19/36 Cesarean section | Living and well, 1943 | Living and normal, 1943 | |
| H. S. 31471 | 35 | 6 months | I | 4/16/37 1,614 mc. h. | 6/24/37 Cesarean section | Living and well, 1943 | Died 18 months Measles | |
| H. S. 31471 | 36 | 4 months | I | 2/10/38 3,204 mc. h. | 7/19/37 Cesarean section | Living and well, 1943 | Microcephaly Died tuberculosis, 8/4/42 | |
| M. L. 33975 | 33 | 4 months | I | 2/25/39 1,752 mc. h. 3/ 4/39 1,001 mc. h. 4/ 2/39 1,169 mc. h. | 6/4/39 Cesarean section | Died July, 1941— recurrence | Microcephaly | 2/13/40—690 mc. h. plus 2,000 r. times 4 |
| J. H. 34894 | 38 | 4 months | I | 10/12/39 1,072 mc. h. 10/16/39 1,064 mc. h. 10/23/39 506 mc. h. 11/13/39 618 mc. h. | Jan., 1940 Cesarean section | Living 3/12/43 | Living and normal, 3/12/43 | |

*Previously reported by Neill.² AM. J. OBST. & GYNEC. 30: 414, 1935.

estimation of the cure rate. There are also probably many cases with spontaneous abortion following treatment which have not found their way into the literature.

These considerations make it impossible to estimate statistically the relative merits and dangers of abortion in the treatment of cervix cancer. It is certain however, that continuation of the pregnancy by no means precludes a cure as indicated by the literature and our own experience. The influence of pregnancy on tumors in general is problematical. The alteration in circulation contingent upon the interruption of pregnancy may exert an unfavorable influence in curing the cervical growth; this possibility is suggested by the very poor prognosis in cases treated at term by necessity with cesarean section, before the treatment of the cervix cancer. It is only fair to say however, that in this latter group the cases are generally more advanced than those seen earlier in pregnancy.

In this discussion very little has been said about the extent of disease in relation to cure. Obviously, this consideration is as important here as in uncomplicated cervix carcinoma. The number of reported cases is too few to make such a correlation of significance. It is to be noted that the majority of prenatal cases is not more advanced than League of Nations Stage II. The neglected extensive cases are not encountered until term when delivery of the child is imperative. In estimating the proper therapeutic procedure in a particular case, due weight must be given to the clinical stage of the disease. One would hesitate to accept for treatment with a view to carrying to term a patient with disease more extensive than Stage II. Because of the pregnancy with its attendant examination most cases will be discovered relatively early.

Technique of Treatment

If it is decided to treat during pregnancy with a view to obtaining a normal living child at term, certain points in technique may be stressed. It is important that no high voltage roentgen-ray therapy be employed because of the obvious dangers of substantial depth dosage in the region of the developing child. Furthermore, it has been our practice to omit the use of tubes within the cervical canal. This is done for the twofold purpose of securing all possible distance from the baby and also to guard against the onset of labor by dilating the cervix. The entire treatment is carried out by tubes held in a cloth plaque against the cervix. The details of treatment in uncomplicated cervix cancer have been previously described.⁴⁰ As an additional precaution against stimulating uterine contractions by prolonged packing against the cervix, we have preferred to use a large amount of radium for a correspondingly short period of time. This means the use of 2.5 to 3 grams of radium. While it is by no means necessary to have available such a quantity of radium for the successful treatment of these cases, the fact that we

have in no case stimulated uterine contractions leads us to believe that this is not an unimportant point.

The dosage is subject to more variation than in uncomplicated cervix carcinoma. This variation is allowable in an effort to spare the fetus all possible treatment and must be determined by clinical experience. In the cases herein reported, the dose varied from 1,614 mc. hr. to 3,922 millicurie hours.

Following delivery it is often desirable to administer additional radium and x-ray.

Operative Treatment

Irradiation is by far the most common method of treatment for uncomplicated carcinoma of the cervix. In spite of this, many cases complicated by pregnancy have been treated by panhysterectomy. This is probably because panhysterectomy seems expedient if abdominal section for delivery of the child is necessary. Nevertheless, one should be hesitant in accepting this as a suitable method of therapy in view of the unsatisfactory results from panhysterectomy in uncomplicated cervix carcinoma even in carefully selected material.⁴¹

The reported cases based on this method are too few to express the cure rate statistically, but Newell and Scrivner,⁴² Stacey and Thompson,⁴³ Stoekl,⁴⁴ Miller,⁴⁵ Chalfont,⁴⁶ Biro⁴⁷ and many others have reported such cases both at term and before with an alarmingly high operative mortality. Furthermore, most of these reports have appeared before an elapsed time of five years so that an estimation of carcinoma of cervix curability is not possible. In our opinion, any necessary abdominal operation either before or following irradiation of cervix carcinoma should be confined to evacuation of the uterus.

Pregnancy at Term

If the baby is viable when the carcinoma is discovered, the problem of injury to the fetus by irradiation need not be considered. Under these circumstances, the child can and often must be delivered by cesarean section. The prognosis under these circumstances has been very poor. There are approximately 40 reported cases to which we have added four treated by various methods including irradiation, panhysterectomy or both; as far as we are aware, the two cases reported by Biro⁴⁷ are the only ones which have survived more than five years. The poor prognosis was in many instances due to the advanced stage of the growth. However, the profound circulatory changes following parturition may be an unfavorable influence in arresting the disease.

The impression received from reviewing the cases of this group, emphasized by the experience of our own four cases, is of a lost opportunity on the part of the attending physician to diagnose and treat an early carcinoma. Almost without exception, the possibility of making an early diagnosis was dissipated by failure to use such simple diagnostic

procedures as speculum examination and biopsy even after the appearance of such an alarming sign as slight vaginal bleeding during pregnancy. Prenatal care through its routine periodic examinations offers an unequaled opportunity to diagnose carcinoma of the cervix at an early stage.

Summary and Conclusions

In formulating a plan for a clinical situation as rare as the association of pregnancy and carcinoma of cervix, one must draw upon the collective experience of the literature as well as upon one's own cases. It is therefore to be regretted that in so many instances, case reports have been issued too soon to be of value in estimating the ultimate outcome either for mother or baby. Many more detailed reports of this condition are needed, but these should not be published before the patient has died, or five years after treatment has elapsed.

We have come to believe that a general rule for the handling of these cases must take into account the obstetric and social background as expressed in the desire of the prospective parents for the child, as well as the extent of the disease. If there are other children, or if the parents do not care to assume the ever present risk of an abnormal child, we see no reason to advise any course except interruption of the pregnancy and adequate irradiation therapy.

The risk of an abnormal fetus cannot be statistically stated at the present time with certainty, but it seems probable that its upper limit is 20 per cent. If the parents and physician for any reason wish to assume this risk, it is justifiable, in our opinion, to proceed with irradiation during pregnancy with a view to obtaining a living child at term. If the pregnancy is at the fifth month or beyond, the risk of an abnormal child is substantially less. As indicated above, the risk to the mother is probably not increased by this procedure as compared with interruption of the pregnancy. The mother's prognosis is intimately related to the clinical extent of the disease. The general experience has been that most cases are discovered early (League of Nations I or II), and the prognosis has been parallel but somewhat lower than for corresponding but uncomplicated groups.

The prognosis of carcinoma diagnosed at term and treated by cesarean section plus panhysterectomy or irradiation, is grave. This is in a large measure due to failure of the attending physician to suspect the diagnosis and apply such simple clinical methods as speculum examination and biopsy, even in the presence of vaginal bleeding during pregnancy.

Case Reports

CASE 1.—O. H., 17355, aged 28, four living children, youngest 3 years. Had irregular vaginal spotting for 3 months. Did not remember missing any periods, but on examination December 18, 1926, she was estimated to be 6 months pregnant. At another hospital, it was thought

that she had a small cervical fibroid which was removed 12/1/26. Pathologic examination however, showed squamous-cell epithelioma. At the examination December 18, the entire cervix was involved and there was some extension of the growth on the vaginal wall. No parametrial extension by rectal examination.

Treatment: 12/18/26—2,644 mc. against the cervix by 7-tube plaque for 40 minutes. Patient went into labor spontaneously 1/16/27 and was delivered by cesarean section. Patient got along very well until 1930, when there was a recurrence. In spite of further treatment with radium and x-ray, the patient died September 12, 1930, from the disease. Female child was examined March 31, 1942, and found to be normal in every way. She was above average in her school work.

CASE 2.—C. B., 22599, aged 32, 3 living children. L. M. P. 12/16/29. Three months prior to May, 1930, there was irregular bleeding and discharge. On examination 5/13/30, it was estimated that she was 5 to 6 months pregnant. On the anterior lip of the cervix, principally on the left side, there was a hard growth. It extended somewhat on to the vaginal wall. Rectal examination showed that there was some induration in the right broad ligament. Biopsy revealed squamous-cell carcinoma.

Treatment: 5/13/30—3,109 mc. by 7-tube plaque against the cervix for one hour. Pregnancy progressed normally and the cervix healed. On September 12, 1930, she was delivered by cesarean section. At operation, the broad ligaments were carefully palpated, and no mass could be felt. Following delivery, there was a recurrence of the normal menstrual flow which was abolished by x-ray in June, 1931. Patient has been examined at intervals since then, the last time being June 12, 1942, at which time she was well. The female child was also examined June 12, 1942, and found to be normal in every respect. She was doing well in her school work.

CASE 3.—A. W., 24792, aged 29. Four normal pregnancies during the last six years. All children living. Patient has never menstruated between pregnancies. In January, 1931, had some spotty vaginal bleeding. There was a little staining each day. In September, 1931, she bled rather profusely for 5 days. First seen November 23, 1931. Abdominal examination showed pregnancy which was estimated to be between six and seven months. Vaginal examination revealed a friable mass confined to the posterior lip of the cervix with no extension on to the vaginal wall. Rectal examination demonstrated no parametrial involvement. Biopsy showed squamous-cell carcinoma.

Treatment: On November 28, 1931, the patient received a 7-tube plaque containing 952 mc. against the cervix for one hour. She was given also four permanent gold radon implants for a total of 20.6 mc. On January 9, 1932, patient received a 5-tube plaque containing 1,606 mc. for 30 minutes. The regression was very satisfactory. On February 11, 1932, a classical cesarean section was performed. At the time of operation no mass could be palpated in the broad ligament region. Since operation, the patient has had no further treatment and is well as of November 1, 1941. The female child was also examined on that date and was normal and getting along in school better than the average for her age.

CASE 4.—S. B., 30042, aged 30. Nine pregnancies and five living children. L. M. P. stated to be October 1, 1935; however, at the time of

examination, February 23, 1936, it was estimated that she was 7 months pregnant. On February 9, she first noted a slight bloody discharge and on February 12, had rather severe bleeding. On the anterior lip of the cervix there was a granular ulcer. There was little or no extension on to the vaginal vault. The posterior lip of the cervix seemed normal. Rectal examination revealed no apparent extension into the broad ligaments. Biopsy showed squamous-cell carcinoma.

Treatment: 1,960 mc. divided into 1 tube in the cervical canal and a 5-tube plaque against the cervix for $1\frac{1}{2}$ hours. Following this, the lesion healed and on April 30, 1936, the cervix appeared grossly normal. On June 5, 1936, a female child was delivered by classical cesarean section. March 12, 1943, mother alive and well, and child living and normal, walked at 11 months.

CASE 5.—H. S., 31471, aged 35, five previous pregnancies; 5 living children. L. M. P. October 8, 1936. First noticed vaginal spotting in the latter part of March, 1937. Never had any irregular bleeding prior to this time. Lost 8 pounds in weight. Examination showed a pregnancy estimated to be 5 months. On the left side of the cervix, there was an ulcer about 2 cm. in diameter. No extension on to the vaginal wall. No involvement of the parametria. Biopsy showed squamous-cell carcinoma of the cervix.

Treatment: On April 16, 1937, received 2,150 mc. against the cervix with a 5-tube plaque for $\frac{3}{4}$ of an hour. Following the treatment, there was rapid healing of the lesion. Cesarean section on June 24, 1937. Following delivery, it was noted that there was some induration of the right side of the cervix. The patient was given an appointment to report back for further treatment but was very slow in doing so and in February, 1938, when she reported for examination, she was found to be again four months pregnant. Biopsy again showed squamous-cell carcinoma which involved the entire cervix but had not involved the vaginal walls or the parametria. On February 10, 1938, she received 2,746 mc. against the cervix for 1 hour and 10 minutes. For a second time, there was a rapid healing of the lesion and at term a second cesarean section was done. She has been followed at intervals since that time, and there has been no recurrence of the growth. The first child died at the age of 18 months. It was in good health until it contracted measles and died. The second child was mentally defective. She entered the Polk (Pa.) State School May 19, 1942. She was classed as an imbecile with an I.Q. of 43. Soon after admission, she showed evidence of active tuberculosis and died August 4, 1942.

CASE 6.—J. H., 34894, aged 38. Four previous pregnancies, the last one 10 years ago. All children living and well. First seen October 12, 1939. Patient complained of intermenstrual bleeding of one year's duration. She was estimated to have a pregnancy of four months. The right side of the cervix was involved in a growth, biopsy of which showed squamous-cell carcinoma. The left side of the cervix was normal, and there was no spread on to the vaginal mucosa or into the parametria.

Treatment: 10/12/39, 1,072 mc. for one hour. 10/16/39, 1,847 mc. against the cervix for 35 minutes. 10/23/39, 1,012 mc. against the cervix for 30 minutes. 11/13/39, 1,236 mc. against the cervix for 30 minutes. There was improvement in the lesion and the patient had a cesarean section in January, 1940. On March 12, 1943, the mother was alive and well, and the child was normal.

CASE 7.—M. L., 33975, aged 33. Patient has 8 living children. L. M. P. October, 1938. First seen February 25, 1939. Examination February 25, 1939, showed a pregnancy which was estimated to be four months. There was a granular growth involving the posterior lip of the cervix and cervical canal. The anterior lip was also thought to be involved as it was stony hard although the overlying mucous membrane appeared normal. Rectal examination showed no involvement of the parametrium.

Treatment: February 25, 1939, 2,628 mc. divided into tube in cervical canal and a 5-tube plaque against the cervix for 40 minutes. 3/4/39, 2,003 mc. similar set up for 30 minutes. 4/2/39, 2,338 mc. with a plaque against the cervix for 30 minutes. Cesarean section June 3, 1939. Careful palpation of the parametrium at the time of operation revealed no induration. The baby appeared grossly normal. There was a recurrence of the growth in November, 1939, and she received a course of x-ray therapy of 8,000 r. through six portals around the pelvis (250 k.v. 30 Ma. 1 mm. copper plus 1 mm. aluminum—15 by 10 portals; 50 cm. S. T. D.; r. measured with scattering). She also received 1,380 mc. for 30 minutes against the cervix. However, she did not do well and died in July, 1941, from the disease. The baby was examined several times and was found to be mentally deficient. By March, 1943, she was not able to talk.

CASE 8.—T. K., 23125, aged 35. August 24, 1930, had normal spontaneous delivery. This was the tenth child. There had been some bleeding during the latter part of the pregnancy. Examination September 23, 1930, revealed the entire vault of the vagina to be filled with a large growth. There was extension into both broad ligament regions but no firm fixation. Biopsy showed squamous-cell carcinoma.

Treatment: October 4, 1930, 3,660 mc. 2 tubes in cervical canal and a 5-tube plaque against cervix for 50 minutes. There was some improvement, but patient died of the disease in July, 1934, in spite of subsequent treatment with x-ray and radium.

CASE 9.—M. H., 24229, aged 38. Multipara 3-0-1-2. L. M. P. September 15, 1930. Pregnancy was normal until February 22, 1931, when she began to bleed in small amounts. Examination June 5, 1931, showed pregnancy of 8½ months' duration. There was a nodular cervix with a growth confined entirely to the portio vaginalis. Biopsy revealed squamous-cell carcinoma. The broad ligaments seemed to be free. As the child was viable, immediate cesarean section was advised and carried out on June 6, 1931. Patient did not receive radium treatment until July 12, 1931. At that time there had been some increase in the size of the growth which was still limited to the cervix. The fornices were clear. There did seem to be some thickening of the right broad ligament region, although at the time of the cesarean section, careful palpation did not reveal any involvement of the broad ligament regions.

Treatment: July 12, 1931, 1,498 mc. for 2 hours with a seven-tube plaque against the cervix.

X-ray 7/16/31, 1,000 r. 7 by 7 suprapubic portal.

7/23/31, 1,000 r. 7 by 7 right lateral and left lateral pubic and 1,000 r. on perineal portal.

7/30/31, 10 by 10 portal 1,000 r. right lateral sacral and 1,000 r. left lateral sacral. Factors as in Case 7.

There was improvement but on September 30, 1931, there was still an ulceration $1\frac{1}{2}$ cm. in diameter which on biopsy showed active growth. Two gold points each containing 6.8 mc. of radon were inserted into this area. On November 1, 1931, patient received 1,060 mc. in the cervical canal for 57 minutes. Patient did not improve and she died of the disease on April 23, 1932.

CASE 10.—E. F., 24280, aged 39. Patient has had 6 children and two miscarriages. All children living. At term the patient had a cesarean section on December 10, 1929, at another hospital. Apparently, it was a classical cesarean section and a supravaginal hysterectomy. It was not until July 25, 1931, that she came under our observation. There had been no bleeding from the time of the cesarean section until May, when it recurred and has continued to the time of examination. A large mass protruded from the cervix and extended on to the vaginal wall. Both parametria were involved to the pelvic wall, and there was fixation to the rectum. It was a very extensive case.

Treatment: July 25 and 26, received 1,000 r. of x-ray through 10 by 10 portals, 9 fields around the pelvis. Factors as in Case 7. August 3, 1931, received 2,673 mc. in and on the cervix for 67 minutes. On August 17, 1931, she died rather suddenly.

CASE 11.—M. K., 34297, aged 31. First seen May 11, 1939. Eight months previously patient had had a cesarean section because of an undilatable cervix. After several hours in labor, there was no progress and section was decided upon. Following this, there continued to be some vaginal discharge until the diagnosis of carcinoma of cervix was made. At this time, the growth was rather massive and had spread into both parametrial regions. Treatment was begun by x-ray and she received 8,000 r. through four portals from May 9, 1939, to May 18, 1939. Factors as in Case 7. On June 1, 1939, 1,212 mc. in and on the cervix for 1 hour. June 22, 1939, 2,361 mc. on the cervix for 35 minutes. Following this, she received many other radium and x-ray treatments, but the growth could not be cured, and she died August 15, 1941.

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OBSERVATIONS ON THE RH-FACTOR IN ITS RELATION TO HEMOLYTIC ANEMIA OF THE NEWBORN INFANT*

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THE work of Levine and his associates¹⁻³ has established the role of the Rh-factor in the pathogenesis of erythroblastosis fetalis. In view of the fact that there still remain problems which have not yet been clarified, the publication of further observations appears justifiable. In agreement with Kariher and Spindler,⁴ Smith⁵ and others, it would appear desirable to abandon the previous terminology such as erythroblastosis fetalis, icterus gravis, congenital anemia and hydrops fetalis which designate some of the clinical manifestations associated with the disease. Since hemolytic anemia is the most important feature the terms, "anemia hemolytica neonatorum, or hemolytic anemia of the newborn," seem appropriate for all forms of the disease. For the sake of brevity it will be represented by the abbreviation, HAN, in this paper.

During the past year, six cases have been investigated from clinical and serological points of view. Because they introduce a number of interesting questions for consideration, they will be described in some detail.

Case Reports

CASE 1.—(Ba.) This mother had five pregnancies. The first child was born in 1937, and is well. The second, born in 1939, had jaundice for the first ten days of life. A red cell count was 4.3 million and hemoglobin, 87 per cent on the third day. These were 5.6 million and 95 per cent respectively, two days later. The liver was slightly enlarged. This child is now well. The third pregnancy, in 1941, resulted in the delivery of a living full-term male infant who died after three hours. Autopsy revealed a ruptured spleen. No jaundice was observed during life or at autopsy. The liver was enlarged. Microscopic sections of the spleen showed hematopoiesis suggestive of HAN. The fourth pregnancy, in 1942, and the fifth, in 1943, both terminated with spontaneous expulsion of a macerated fetus of about five months' gestation. No microscopic study of organs was possible. Blood grouping† of the living members of the family after the last miscarriage was as follows:

| | Group | Rh |
|----------|-------|----|
| Father | A | + |
| Mother | B | - |
| Son | A | + |
| Daughter | AB | + |

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†The technical procedure employed for the determination of Rh constitution was that recommended by the Blood Transfusion Association of New York, in the pamphlet, "Instructions concerning the use of human anti-Rh serum."

The serum of the mother tested against several samples of Rh-positive and Rh-negative red cells demonstrated the presence of anti-Rh agglutinins. Tests for α agglutinins revealed a titer of 1:1,024. Two months later, the findings were the same. After four months only traces of anti-Rh agglutinins could be found and the titer of α agglutinins fell to 1:128.

CASE 2.—(Fr.) This mother had one normal living child. Two and a half years later, in 1943, a second infant, a boy, was born at term. He showed jaundice half an hour after birth. Four hours later jaundice was intense and the spleen and liver were enlarged. Two transfusions with blood from the father were given in the course of 24 hours. The infant died when 48 hours old. Necropsy showed characteristic extra-medullary hematopoiesis as well as selective jaundice of basal ganglia of the brain (kernicterus). On the first day of life a red cell count was 1,980,000 and hemoglobin, 43 per cent, and on the second day these were 2,050,000 and 43 per cent, respectively.

Blood grouping of the family was:

| | Group | Rh |
|---------------------|-------|----|
| Father | O | + |
| Mother | A | - |
| First child (male) | A | + |
| Second child (male) | O | + |

The serum of the mother contained anti-Rh agglutinins to a titer of 1:8. The titer against B cells was 1:32.

CASE 3.—(Ju.) The mother had five healthy children. The neonatal histories of the first two make no mention of jaundice. The third developed jaundice on the third day of life. It lasted four days. The fourth child had intense icterus which appeared on the third day. The blood showed normoblasts. The red cell count dropped to 2,700,000 after two weeks. No transfusion was given. Recovery took place slowly. The liver, which was enlarged, eventually returned to normal size. The fifth baby, male, developed deep jaundice the day after birth. This increased until the third day and cleared up after seven days. The red cell count dropped to 2,500,000 and hemoglobin, to 50 per cent on the seventh day. A transfusion was given. The next day the red cell count had risen to 3,800,000 and hemoglobin, to 75 per cent. As was later ascertained, the donor used was fortunately Rh-negative. Stained films of blood did not reveal any erythroblasts. One and a half years later the child was normal. At this time blood grouping of the whole family was performed.

| | Group | Rh |
|-----------------------|-------|----|
| Father | B | + |
| Mother | A | - |
| First child (female) | B | + |
| Second child (male) | A | - |
| Third child (female) | A | + |
| Fourth child (female) | A | + |
| Fifth child (female) | O | + |

The serum of the mother showed anti-Rh agglutinins to a titer of 1:64 still present one and a half years after the last delivery. The titer of β agglutinins was 1:256.

CASE 4.—(Ol.) A first baby, male, was born spontaneously at term. Eight hours after birth, pronounced jaundice was observed. At the

same time, cyanosis appeared and breathing became labored. The jaundice increased steadily. The spleen became palpable. The infant died after 48 hours despite a transfusion of thrice washed red cells suspended in normal saline. The cells were obtained from the mother's Rh-negative blood. Examination of the infant's blood showed 2,100,000 red cells, 60 per cent hemoglobin, 129,000 white cells (including normoblasts). Numerous normoblasts were seen in stained smears. Blood grouping of the family was:

| | <i>Group</i> | <i>Rh</i> |
|---|--------------|-----------|
| Mother | O | - |
| Child (male) | A | + |
| Father could not be typed as he is overseas. | | |

The mother's serum contained anti-Rh agglutinins to a titer of 1:4. The titer for α agglutinins was 1:8, for β agglutinins, 1:256. Two months later only traces of anti-Rh agglutinins could be found. Serum from cord blood was also tested for the presence of anti-Rh agglutinins. Tests with known red cells were set up in the usual manner. No agglutination could be seen either with a magnifying lens or under the microscope. A large drop of the mixture was placed on a glass slide and reincubated for two hours. By this method, weak agglutination could be seen with all the Rh-positive cells whereas the Rh-negative cells did not show any clumping. This effect could not be produced by using only the slide method.

The history of the mother revealed that she had received seven transfusions during one month in the course of a general septicemia four and a half years previously. It was impossible to test the donors for their Rh constitution, but it seems reasonable to assume that most if not all were Rh-positive. No severe reactions following the transfusions are reported, but it is stated that after the last three, a slight chill took place and after the fifth transfusion, the urine became dark red in color.

CASE 5.—(Be.) The first two children born to this mother in 1928 and 1932, respectively, were normal at birth and are now well. The third pregnancy, in 1938, terminated normally with a living male child. Thirty hours after birth, pronounced jaundice was noted. This persisted until death. The red cell count was 4,400,000 and hemoglobin 76 per cent on the third day and these dropped to 1,350,000 and 41 per cent respectively, on the twentieth day, just before death, despite six transfusions, which at that time were given without regard to the Rh-factor. Fever was present on the fourth and fifth days and during the last week of life. Necropsy revealed generalized jaundice. The liver and spleen were enlarged. There were multiple small abscesses in the lungs and liver. No extramedullary hematopoiesis was seen. A fourth pregnancy in 1939 terminated in a breech extraction of a macerated fetus of approximately 7½ months' gestation. Pathologic examination, which was done a few days later, showed extensive autolysis. The fifth pregnancy, contrary to expectation, went to full term ending in the delivery of an apparently normal male infant. Two days after birth jaundice was noticed. This increased for some days and disappeared by the thirteenth day of life. The red cell count dropped from 5,300,000 on the first day to below 2,000,000 on the fifth day. It increased after two transfusions with washed Rh-negative cells, but fell again to 1,600,000 on the thirteenth day.

Another similar transfusion was given after which the red cells increased to 2,100,000. From then on the red cell count gradually improved. Four to six nucleated red cells were seen on the second day; subsequent films of blood showed 0 to 3. When seen two months later, the infant was almost normal. Blood grouping of the whole family gave the following picture.

| | Group | Rh |
|----------------------|-------|----|
| Father | O | + |
| Mother | O | - |
| First child (female) | O | + |
| Second child (male) | O | + |
| Third child (male) | O | + |

The mother's serum contained anti-Rh agglutinins to a titer of 1:32. The titer for α agglutinins was 1:64 and for β agglutinins, 1:16. Cord blood tested as described previously did not reveal any anti-Rh antibodies.

CASE 6.—(Fa.) The first pregnancy in 1936 terminated with the birth of a normal male infant. A second pregnancy in 1943, ended with the delivery of a male baby. Routine testing of mother's and infant's blood during the course of studies proceeding in this hospital revealed that the mother belonged to group AB, Rh-negative, and the infant to group AB, Rh-positive. An immediate test for anti-Rh agglutinins in the serum of the mother gave a strongly positive result, the titer being 1:1,000. At this time, no clinical signs of HAN were observed. A few hours later, jaundice became obvious. A red cell count was 5,025,000 and hemoglobin, 106 per cent. No erythroblasts were seen in stained blood smears. The next day the red cell count had dropped to 3,900,000 and hemoglobin to 92 per cent. A transfusion of washed cells obtained from the mother's blood was given that day and another the following day. Thereafter a red cell count of around 4,800,000 and a hemoglobin level of around 100 per cent were maintained until the eighth day of life, when the jaundice had cleared up. A further drop in the red cell count to 3,416,000 and hemoglobin to 84 per cent by the eleventh day was an indication for another transfusion. Rh-negative whole blood was used. The next day a red cell count was 4,920,000 and hemoglobin 109 per cent, but at the same time jaundice reappeared and remained for two days. When discharged from the hospital, the infant was pale but no jaundice was evident. The red cell count was 4,000,000 and hemoglobin, 83 per cent. Anti-Rh agglutinins of a low titer were found in the breast milk but not in the saliva or urine of the mother, or in cord blood. Blood grouping of the family was as follows:

| | Group | Rh |
|---------------------|-------|----|
| Father | B | + |
| Mother | AB | - |
| First child (male) | B | + |
| Second child (male) | AB | + |

Comment

These observations on six families represent many features of HAN. Common to all cases that could be tested (only one father was not available) was the combination of an Rh-negative mother, an Rh-positive father, and child. All the mothers had anti-Rh agglutinins in their sera to a higher or lesser degree.

The sex distribution of six known cases was four males, 2 females. If seven presumptive cases are added to these making a total of 13, ten were male and three female. Although this would appear to indicate a predilection of the male sex, the small numbers do not warrant any definite conclusion. Potter⁶ reported 23 males and 13 females in 36 autopsies of infants who died of HAN.

Case 1 presents a typical history of HAN with increasing damage in successive pregnancies. The high titer of 1:1,024 for α agglutinins in the mother's serum is noteworthy. Apparently there was immunization not only by the Rh factor, but also by the normal iso-agglutinogens.

Case 2 demonstrates the ineffectiveness and possibly an injurious effect of transfusion with Rh-positive blood.

Case 3 shows that even after repeated immunization by 3 previous pregnancies with Rh-positive children, it does not necessarily follow that a severe form of HAN will ensue. In spite of the fact that agglutinins were demonstrable one and a half years after the last delivery, suggesting that the antibodies at the time of the pregnancy must have been of high titer, the infant made a satisfactory recovery.

Case 4 reveals the harmful effect of transfusions with Rh-positive blood to an Rh-negative woman. Although the transfusions (7 in the course of 4 weeks) did not cause any dangerous reactions in the patient herself (possibly the time interval between the first and last transfusions was too short), they were sufficient to immunize her to such a degree that her first child died of HAN 36 hours after birth in spite of a transfusion with Rh-negative blood. That immunization of the mother by transfusions rather than by the fetus was responsible for the severity of the disease in this case is supported by the fact that the iso-agglutinin titer for α agglutinins was only 1:8, and for β agglutinins 1:126. The child belonged to group A. This is in sharp contrast to case 1. Apparently very little if any A antigen passed through the placenta and the same is suggested for the Rh factor. It seems unlikely that only one of two antigens present should have passed into the maternal blood stream. That the A and B agglutinogens are able to immunize is shown by the rise of the corresponding agglutinins after transfusion with incompatible blood.

Two similar cases have been reported by Diamond⁷ in one of which the offspring was afflicted with HAN even though the mother had previously received only one transfusion. It is therefore highly desirable that no female of Rh-negative constitution should be transfused with Rh-positive blood. Otherwise, her potential offspring may be endangered and possibly her chance of having a living child destroyed. Taking such precaution would of course also prevent the possible occurrence of a reaction due to anti-Rh agglutinins if she should subsequently happen to be transfused with Rh-positive blood.

Case 5 illustrates a well-known course of events in the first four pregnancies, i.e., a gradual increase in the severity of HAN. However, it is

interesting that the fifth pregnancy ended with a full-term living infant. The high titer of anti-Rh agglutinins, 1:64, found in the mother's serum is evidence that a considerable amount of antibodies had been produced by her.

In Case 6 the interesting features are the exceptionally high titer of anti-Rh agglutinins, 1:1,000 in the mother, and the fact that after the third transfusion with compatible Rh-negative blood (which was tested with a standard anti-Rh serum as well as with the mother's serum), jaundice reappeared in the infant. This suggests the possibility of a sudden massive destruction of red cells. This occurrence may possibly be explained by the use of fresh whole blood containing complement. The possible role of complement in the clinical picture of HAN will be considered later.

Discussion

The evidence so far accumulated supports the theory that HAN is brought about by the following sequence of events. As a result of the passage of Rh-positive blood from the fetus through the placenta into the maternal blood stream, anti-Rh antibodies are produced in her. These maternal antibodies are then transmitted through the placenta in the opposite direction from her to the fetus and hemolyze fetal red cells. Ninety per cent of cases fit into this explanation, and in the remaining ten per cent, it is assumed that other similarly acting antigen contained in the fetal red cells is responsible for the condition. It is interesting to speculate as to the mechanism which allows fetal Rh-positive red cells to immunize the mother whose blood is Rh-negative. It does not seem probable that whole red cells of the fetus would penetrate the placental barrier and enter the maternal circulation unless some pathologic condition permits of their passage. In this connection Javert⁸ has reported the presence of hematomas in the intervillous spaces of 8 placentas out of 35 in cases of HAN. This is a rather low incidence, and furthermore, no control studies are mentioned as to the presence or absence of such lesions in instances in which the combination of an Rh-negative mother and an Rh-positive infant occurs without accompanying HAN. In the absence of some placental lesion, the red cell is probably too large to pass through the meshwork of reticulum but soluble proteins, antigenic in nature, might do so. It is possible that these soluble proteins contain the Rh antigen. A similar situation pertains to subcutaneous injections of bacterial vaccine. Following injection the organisms are not found in the blood stream, yet antibodies are produced against them. It seems likely that soluble antigenic protein molecules of very small size might find their way through the reticulo-endothelial system into the blood stream, and so stimulate the production of antibodies. The fact that only 2 to 4 per cent of Rh-negative mothers give birth to infants who present evidence of HAN, lends credence to the view that the Rh-factor may be of very small dimensions, and might therefore be a

weak antigen when administered intravenously.⁹ Mothers may also vary in their ability to be immunized by the Rh-factor. However, a massive dose of antigen as a result of transfusion does immunize a resistant mother. Thus, Diamond⁷ has reported an interesting observation of an Rh-negative woman who had four healthy children who were all later proved to be Rh-positive. She received a transfusion of blood from her husband who was Rh-positive with no apparent untoward effect. A child born following this had typical HAN, suggesting that immunization took place as a result of the transfusion rather than the preceding pregnancies.

Another point worthy of consideration is the variation in the clinical picture of HAN. It is reasonable to suppose that the amount of hemolysins produced and the amount transmitted to the fetus and the time when such transmission occurs will have an important bearing on the clinical manifestations of the disease. If hemolysis begins early in fetal life, miscarriage, premature birth, or stillbirth may occur; whereas, if a considerable amount of hemolysins is acquired later, i.e., toward the end of pregnancy, an apparently healthy infant may be born at full term and signs of HAN may not become evident until some time after birth. Indeed, a red cell count and hemoglobin determination just after delivery may show the presence of a slight anemia. This is usually overlooked since such examination is rarely done at this time.

It is a common observation that hemolysis may set in and progress after the cord is cut, and any further transmission of hemolysins is impossible. It has been suggested that the hemolysins are stored in the fetal tissues and so rendered innocuous for the time being, and that for some unknown reason, they are released after birth.^{5, 10} Wiener and Wexler¹¹ imply that only when these storage places are filled to capacity during fetal life will the disease start in utero. According to Kariher,¹² the end products of red cell destruction are eliminated from the fetus in utero by means of an interchange of substances through the placenta, whereas after birth, they are accumulated in the infant. This could explain why jaundice may appear some time after birth, but not why some infants show severe jaundice at birth, and why the destruction of red cells may make such rapid progress in the first days of life and sometimes continue for weeks.

Hemolytic reactions as a result of α and β hemolysins as well as anti-Rh hemolysins are usually observed shortly after transfusion. It is difficult to understand why anti-Rh hemolysins should show a completely different behaviour in the fetus. The theory that they are stored away in the tissues, or in the reticulo-endothelial cells has been offered by Wiener and Wexler.¹¹ A different hypothesis may be proposed as an explanation. It is known that the amount of complement varies not only as between different persons, but also in the same person at different times. It is not known how much complement exists in the fetus, whether it is transmitted from the mother similar to antibodies, or when the fetus

begins to form it. It has been determined that the amount of complement in cord blood¹³ and in the first days of life^{14, 15} is distinctly smaller than the quantity found a short time later. There is also a wide variation between different cord sera. This comparatively small amount of complement in early life could explain the relatively slow action of the hemolysins in HAN as compared with their quick action in reactions following transfusion. Complement may have played a role in Case 6 where a recurrence of jaundice was observed after fresh Rh-negative whole blood was transfused.

Lack of complement would account for the fact that hemolysis may increase relatively slowly after birth, but it does not explain the fact that it may extend over a period of weeks. An explanation of this occurrence may be offered by some experiments of Pfeiffer and Friedberger,¹⁶ and Bail and Tsuda¹⁷ who noted that vibriolysins are not completely utilized by the process of vibriolysis in the peritoneal cavity of the guinea pig, but are set free after the destruction of the vibrios and can exert their action again. The authors concluded that no consumption of vibriolysins could be demonstrated by the process of lysis. These experiments differ from those of Bordet.¹⁸ Pfeiffer¹⁹ explained this difference by pointing out that Bordet performed his experiments with hemolysins in the test tube where no complete destruction of the red cell occurs, but only a bursting of the membrane, liberating cell contents, and that the stroma retains bound antibodies. However, in the living animal complete destruction of vibrio takes place. It is possible that the same may happen in the case of hemolysis occurring in a living body. If this could be shown to be so, it could explain persistence of the hemolytic process in the baby until the hemolysins, like any other passively introduced antibodies, are eliminated from the body. Since the serum containing the antibodies is of homologous character, it might tend to lengthen the period of elimination. Schütze²⁰ found that vibriolysins were present in passively immunized guinea pigs after 24 days, if homologous serum was injected whereas, if heterologous serum was used, they were present for only 6 or 7 days.

Until a few years ago, the diagnosis of HAN was made purely on clinical and hematological grounds. As a result of Levine's discovery, it is possible to anticipate its occurrence and thus make an early diagnosis, in some instances before clinical signs become evident. Determination of the Rh constitution of an expectant mother may be done at the same time as a sample of blood is drawn for a Wassermann or similar test. If she is Rh-negative, a test of the husband's blood will reveal the possibility of immunization by Rh antigen. If he is Rh-positive, his wife's serum may be tested shortly before the calculated time of delivery for the presence of anti-Rh agglutinins using the husband's red cells preferably for this test. If this blood cannot be used due to group incompatibility, any compatible Rh-positive cells may be employed. If the presence of anti-Rh agglutinins is demonstrated HAN may be suspected. Furthermore,

in all instances in which the mother is known to be Rh-negative, the presence or absence of Rh factor in her newborn infant should be determined immediately after birth. This can be done quite easily by using a sample of cord blood. If it is Rh-positive, the baby should be watched closely and have repeated hematologic examinations so as not to miss the first signs of the disease.

As reported by other observers,^{11, 21} there was no correlation between the titer of anti-Rh agglutinins in the mother's serum at the time of delivery and the severity of the disease in her newborn infant. A very severe case was associated with a low maternal anti-Rh agglutinin titer and a mild or moderate one, with a very high titer. To account for this Wiener and Wexler¹¹ offer, the theory previously mentioned of storage of anti-Rh antibodies in the tissues, it might be explained in the following manner:

1. Only a fraction of the antibodies normally present in the mother's blood passes through the placenta into the fetal circulation. The size of this fraction varies and seems to depend upon the permeability of the placenta. Titrations of mother's and corresponding cord sera for iso- as well as hetero-agglutinins were performed. These showed that the percentage of transmitted antibodies varies considerably. Two of the most striking examples are given in Tables I and II.

TABLE I. TITRATION OF HETERO-AGGLUTININS (SHEEP CELLS)

| SERUM OF | DILUTION OF SERUM | | | | | | | | | |
|---------------|-------------------|-----|-----|-----|------|------|------|-------|-------|-------|
| | UNDILUTED | 1/2 | 1/4 | 1/8 | 1/16 | 1/32 | 1/64 | 1/128 | 1/256 | 1/512 |
| No. 45 Mother | 4+ | 4+ | 4+ | 3+ | 2+ | 1+ | - | - | - | - |
| Baby | 4+ | 4+ | 4+ | 2+ | ± | - | - | - | - | - |
| No. 63 Mother | 4+ | 4+ | 4+ | 4+ | 4+ | 3+ | 2+ | 1+ | - | - |
| Baby | 1+ | - | - | - | - | - | - | - | - | - |

TABLE II. TITRATION OF ISO-AGGLUTININS (BETA)

| SERUM OF | DILUTION OF SERUM | | | | | | | | | |
|---------------|-------------------|-----|-----|-----|------|------|------|-------|-------|-------|
| | UNDILUTED | 1/2 | 1/4 | 1/8 | 1/16 | 1/32 | 1/64 | 1/128 | 1/256 | 1/512 |
| No. 6 Mother | 4+ | 4+ | 4+ | 4+ | 4+ | 4+ | 4+ | 3+ | 2+ | ± |
| Baby | 1+ | ± | - | - | - | - | - | - | - | - |
| No. 76 Mother | 4+ | 4+ | 4+ | 4+ | 3+ | 1+ | ± | - | - | - |
| Baby | 4+ | 4+ | 2+ | 1+ | - | - | - | - | - | - |

2. The second and probably more important consideration is that we measure agglutinins in the test tube, whereas the determining factor in the body is the hemolysin. The power to agglutinate in vitro does not always correspond with the power to hemolyse in vivo. The same discrepancy between agglutinating and lytic effect exists in other sera. Anticholera rabbit serum, made with a single injection of $\frac{1}{10}$ loop of vibrios, usually has a high vibriolytic effect in the peritoneal cavity of guinea pigs, and often a low agglutination titer in the test tube.

The treatment of choice for HAN is early transfusion with a concentrated suspension of Rh-negative red cells. If the mother's serum contains anti-Rh agglutinins, it would seem desirable not to delay transfusion until the red cell count and hemoglobin drop much below normal. The number of transfusions will depend upon the course of the disease. In many cases two or three will be sufficient to carry the baby over the critical time. It is now generally agreed that only Rh-negative blood should be used since Rh-positive cells will undergo the same destruction as the cells of the infant and the resulting increase in bilirubinemia will place a further load on an already overburdened liver. Whole blood of even an Rh-negative donor should not be given if that person has ever received a transfusion of Rh-positive blood, or, in the case of a woman, given birth to an Rh-positive child. To test for the presence of anti-Rh agglutinins in such prospective donors' sera is not sufficient as hemolysins may be present which are not detected by the agglutination test. If such donors have to be used, their red cells should be washed and suspended in saline, or inactivated plasma of the same blood group. Treated in this manner, even the red cells of the mother herself can be given without danger. In the rare cases of HAN, where mother and newborn are both Rh-positive or both Rh-negative, washed red cells of the mother are the only ones which can be transfused safely, as it might be difficult, or impossible to determine the specific antibodies at fault, and to select suitable donors. Transfusions of washed red cells have been used in the treatment of HAN by Wiener and Wexler,¹¹ Brown and Levine,¹⁰ and others. Levine²² states it is probably not necessary to wash the mother's Rh-negative blood for the complete removal of her plasma. Red blood cells can be concentrated to the desired level, and possible transfer of antibodies and complement, which may be present and may prove to be harmful, is excluded. Transfusions of concentrated suspensions of red cells are recommended by Watson²³ and others, who found it to be satisfactory when the aim is to increase the oxygen-carrying capacity of the circulating blood. It is especially valuable when it is desired to obtain the maximum rise in hemoglobin with the injection of a minimum of volume.

Summary

In six families there occurred six cases of hemolytic anemia of the newborn, and there was evidence that seven other infants had probably suffered from this disease.

Common to all cases tested was the combination of the following conditions: The mother was Rh-negative, the father was Rh-positive (only one father was not available for testing), and the infant was Rh-positive. All the mothers had anti-Rh agglutinins in their sera.

Immunization of an Rh-negative woman by repeated transfusions of presumably Rh-positive blood was later followed by fatal hemolytic anemia of her first newborn infant. Rh-negative females should not be

transfused with Rh-positive blood to prevent the possibility of this undesirable effect upon any future Rh-positive offspring.

A possible role of complement and of the liberation of hemolysins after the destruction of red blood cells in the clinical picture of HAN is discussed.

No correlation was found between the titer of anti-Rh agglutinins in the mother's serum at parturition, and the severity of the disease in her newborn infant.

As the treatment of choice for this disease, the infant should receive a transfusion of a concentrated suspension of washed Rh-negative red blood cells as early as possible, and this should be repeated as often as may be necessary. A suspension of washed cells from the mother's blood may be used if no suitable donor is available. Washed cells from the mother's blood should be used in any case where the mother and her newborn infant who shows evidence of the disease are both Rh-positive or both Rh-negative.

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PSYCHODYNAMIC AND THERAPEUTIC ASPECTS OF FUNCTIONAL DYSMENORRHEA

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IN VIEW of the tremendous strain on feminine emotions, and the ensuing psychic stress caused by the impact of the war in general, the subject of dysmenorrhea is becoming one of growing importance. It is to be assumed that this complaint occurs not only as a result of certain irregular anatomic and pathologic conditions, but may appear in consequence of some psychic disturbance. Needless to say, the psychologic equilibrium of a woman may be adversely affected by other than war emergencies, and neurotic manifestations may well be the result of other disturbing experiences in her life.

Possible Neurotic Origin of Dysmenorrhea

It is the purpose of this article to point out the close relationship between dysmenorrhea and neurosis. A neurosis may be the sole or predominant cause of dysmenorrhea, or it may mold the signs and symptoms associated with gynecologic features exclusively.

There is a consensus of opinion that menstruation, as a physiologic phenomenon, should be free of any organic or mental discomfort; causes of the menstrual suffering are open to discussion. In the last few years, there is increasing evidence that any consistent anatomic lesion is absent (Julius Bauer,² Randall and Odell⁸). Psychic factors as the pathogenic principle are surmised by a growing number of authorities. Fairbairn⁴ confirms this claim by discussing the results of cervix dilatation. Kurzrok,¹¹ after having meticulously evaluated the endocrinologic aspects, is in favor of some psychic mechanisms. Similar conclusions were drawn by Emil Novak⁷ and Leon Israel.⁵ Space does not permit a complete list of all researchers whose work finally led to the same conclusion.

The psychotherapist feels that these testimonies do not substantiate the psychogenesis. He is in a position to furnish a workable theory which explains some dynamics of functional dysmenorrhea together with its concomitants; he can further explain why the different remedies and operations have an influence on the patient, not on her genitals, but on her personality as a whole. By approaching this problem, he chooses the means of the psychomotor reflex.

Psychomotor Reflex

It is understood that emotions are psychic acts provoking bodily features; these features are specific for any given emotion, and their

purpose is to clear away the tension resulting from any emotion. The unity emotion and bodily reaction is spoken of as psychomotor reflex.

Any one of the numerous qualities characteristic for neurotics is likely either to disturb a "normal" psychomotor reflex, or establish a new one under conditions alien to the normal being. Neurotics show vivid associations, they connect certain facts with experiences and vice versa. Therefore, menstruation is being connected with certain old events, experiences, queer ideas. Emotions, primarily belonging to this old material, are attributed to menstruation. In her dysmenorrhea, a woman is reminded of some situation of her past and, at the same time, is prevented from realizing this situation. This explanation is based on the concept of the unconscious which makes simple, logical explanation of this dependence ineffective to the sufferer. For that reason, a neurotic is never capable of correcting her misconceptions by experience.

The origin of dysmenorrhea is the (neurotic) belief that menstruation, a phenomenon of so great an importance and impact must afflict the sphere of feeling. Anxieties and fears are experienced, because some repressed material is touched upon; the neurotic associates anxiety with menstruation, thus establishing the vicious circle.

History

This assumption is corroborated by a dysmenorrheic girl's history. The most bewildering reports of her first menstruation can be obtained. She was caught by surprise, had no idea about its purpose, and reacted with fear of death. Opportunities to observe her older sister's menstruation were not utilized or, if experienced, completely forgotten under the impact of this frightening event. It is further astonishing how this girl's mother allegedly reacted to her daughter's first menstruation. She did just the contrary of what would be expected to appease the youngster's fears. It is obvious that tales like these are true only in exceptional cases; the psychologist must base his investigations on these fantasies, he must take them for granted. The truth will be found out later.

Another frequently reported reaction is the conviction that the patient has been wounded or mutilated. The bleeding is expected to be fatal. According to her temperament, a girl may respond with hyperactivity or lethargy. To boyish girls, the first menstruation means inevitable and mortifying womanhood, a fate against which they have been struggling all their lives. Finally, some girl was put into bed by her overanxious mother, thus pervading her with apprehensions.

Closer investigation shows the reasons for this behavior. It is the strict consequence of older experiences, either real events (trauma), or any condition which afflicted a girl adversely. That a parent's death

may act as a trauma, is undoubted. The same holds true for sexual experiences. One needs not think of some violent and terrible sexual scene; a mere trifle may act as strongly and lastingly as any real trauma. Arguments or dissensions in the parent's home, unhappy marriage, drunkenness or infidelity of a parent may call forth either protestation against her female role, or abhorrence of menstruation. These facts have shaped the conviction that menstruation and sickness are identical.

Clinical Symptoms

Dysmenorrhea is an organ neurosis, i.e., it is referred to suppressed material and shows the following characteristics of functional disease:

A. *Absence of an Underlying Pathological Anatomical Process.*—Since we were able to correct the conception "Nulla dysmenorrhea nisi obstructiva," no other organic cause was generally accepted as being present. This fact is supported by:

B. *Inconstancy of Pain.*—The degree of pain varies from month to month in the same individual, mostly as a reaction to pleasant or to distressing events.

C. *Reversibility.*—This is the outstanding characteristic of any neurotic symptoms. The entire process may be reversed, the body recovering its original normal function, no trace being left to show that a pathologic condition had ever been manifested.

D. *Connection With Other Neurotic Symptoms.*—(1) When a psychologic cure has been effected in a neurotic woman, menstrual cramps disappear, even when no treatment has been administered for the latter. This was first stated by Allers.¹ (2) In concentrated psychotherapy, multiple connections were found between dysmenorrhea and almost every neurotic symptom of the patient, a point more fully referred to later.

E. *Amenability to Various Medical Measures.*—In addition to the pronouncements of various authorities, it may be stated that at one time or another, a variety of drugs have been successfully employed in the treatment of dysmenorrhea.

F. *Suggestion and Hypnosis.*—This important curative process has been described by many investigators. Hypnosis, the most effective form of suggestion, has been found to bring about a complete cessation of dysmenorrheic cramps in a great many cases. Its employment, however, because of the attendant dangers inherent in the hypnotic procedure, is not recommended.

Sequelae

The neurotic element alters the symptomatology, complicates the disease, and renders it more difficult of diagnosis and cure. On the

other hand, there are cases in which the neurosis effects the disappearance of the dysmenorrhœic syndrome, in which the following aspects can be observed.

1. *Development of the Complete Picture.*—Cramps are in the foreground, the menstrual lochia may be changed (duration, quality, and amount), premenstrual discomfort can be observed and other neurotic symptoms harass the patient.

2. *Stationary.*—There is little to say about those women who tolerate discomfort and attribute their pains to womanhood. In the words of a novelist, they regard themselves as the "Slaves of the Moon."

3. *Changeable.*—The amount of pain varies during each period, and the patient can give no reason for this change. A scrutiny of the history, however, reveals the fact that the degree of pain varies regularly with some pleasant or unpleasant experience. For example, a word of praise from her employer may cause the pain to diminish, while excitement precipitated by discord between the patient and her husband or mother may bring about an increase in the severity of the pain.

4. *Disappearance of Dysmenorrhea.*—In the majority of cases this occurs either through the influence of sexual activity, pregnancy, etc., or through fortuitous circumstances of minor importance. Cases of spontaneous (untreated) disappearance deserve the fullest attention, because in these, while the symptom is removed, the underlying cause persists and is apt to produce some other symptom, either organic or neurotic in character. It remains to be demonstrated whether there is a relation between the "cured" dysmenorrhea and the symptom which follows the cure. In such cases the appearance of diarrhea, constipation, gastric discomfort, heart palpitations, migraine, etc., can be observed. The development of certain compulsions is also quite frequent, especially an exaggerated desire for self-cleansing. Depression is another quite common substitute, or a slight loss of sexual feeling, when freed from cramps.

5. *Recurrence of Dysmenorrhea.*—As is well known, dysmenorrhœic cramps sometimes reappear after a period of cessation. Frequently, this fact is overlooked if it occurred prior to gynecologic examination, yet a knowledge of it is valuable in arriving at a clear understanding of the patient's history.

I had occasion to observe such a recurrence in a patient who, at the time of re-experiencing cramps, was not menstruating.¹⁰ She was thirty-three years old, unhappily married, and the mother of three children. Her cramps had stopped after her first confinement. Her sexual feeling was unstable, she was able to experience full climax only by masturbating, but never during intercourse, for she had imagined, unconsciously, that there was something in her womb. When, in the course of treatment, this unknown something was determined by eliciting the traumatic situation, her cramps reappeared, without menstruation.

It has been the experience of many investigators that complete cures can be effected more often and with greater ease among young patients than in cases where dysmenorrhea has been present for a long time. A variety of treatments have brought about cures, particularly when the treatment dealt with the causes basically responsible for the illness of the individual. Some physicians are excellent psychologists by nature, and are thus able to choose promptly the most appropriate procedure. Many other conditions may also be helpful in working toward an elimination of the symptom as, for instance, the patient's growing weariness with it, or else, the relation between the gynecologist and his patient (Freud's term, "transference"), or any occurrence which tends to wipe out the pathogenic neurotic idea underlying the dysmenorrhea. Psychologically speaking, this group presents monosymptomatic neuroses, an expression which is easily understood.

Definition of Dysmenorrhea and Its Concomitants

In accordance with the above concept, it is proposed to include in "functional dysmenorrhea" a symptom complex associated with menstruation which affects, in addition to the pelvic organs, the personality as a whole. It would appear that all features manifested by the dysmenorrheic patient seem to be suppressions and conversion symptoms. All symptoms are closely interrelated and each supports and perpetuates the other; thus constituting a vicious circle which can be broken on either the physical or psychological level.

Dysmenorrhea may manifest itself in three different spheres:

Local.—Cramps; duration and intensity of flow; quality of the lochia accompanied by a feeling of heaviness in the regions of the uterus, pelvis, groin, backbone, etc., disturbance of urination as frequency, retention or incontinence; and of the defecation, as constipation or diarrhea.

General.—Manifestations in other organs which show a temporary and casual connection with the menstruation, i.e., in the stomach (anorexia, change in appetite), all forms of headache, heart symptoms of a neurotic character, etc. The secondary sexual characteristics at different sites of the body may be involved both organically and psychologically (skin, mammary glands).

Psychosexual.—Mental fatigue, anxiety, compulsion-like features, hypochondriacal symptoms, aggressiveness, craving, etc., are indications of menstrual disturbances. The sexual desires and impulses often become modified to the extent of being completely reversed, thus generally affecting the libido as to its intensity, direction, and form of expression.

In the psychologic approach it is essential to make a distinction between primary and secondary dysmenorrhea, as the former offers more resistance to psychotherapy than does the latter. Primary dysmenor-

rhea begins with the menarche, while secondary dysmenorrhea appears after a number of normal painless menstruations.

This definition of dysmenorrhea should shed light upon a number of complex questions of great importance which puzzle the physician. As stated, there is little significance in the cessation of the menstrual cramps in the majority of cases. The underlying cause persists, while the form of its expression takes another aspect. This may result in a new symptom giving rise to disorders of varying intensity, which often crop up only after a certain lapse of time. An occurrence in a patient's life, causing strong emotion may call forth the new symptom, especially if the event holds symbolic meaning and has any relation to those repressions which provoked the original dysmenorrhea. A state of anxiety may follow an operation, an abortion, or confinement, although this does not always occur. Women passing through the menopause may also be similarly afflicted. The death of a child, or any frustration, may become the cause of a neurotic condition which, in turn, may progressively transform itself into a psychosomatic phenomenon. The following observation will serve to demonstrate these points.

Psychotherapeutic Cure

CASE 1.—A colored woman, single, and twenty-eight years of age suffered from menstrual disturbances which consisted of fainting spells, vomiting, urinary frequency and severe cramps which confined her in bed during the first two days of her menstrual periods. Following a nervous breakdown, six months before the first interview, she had been stricken by these symptoms during each period.

Her first menstruation, which occurred at the age of thirteen, had surprised and bewildered her, and finally impressed upon her the terrible fear that she would bleed to death. She tried to clear the blood away by washing her genitals. Her grandmother comforted her, and gave sanitary advice and enlightenment about the menstrual cycle. The subsequent menstruations were accompanied by some pain which, by the time she became eighteen, was rather distressing. As she spoke, the patient uttered concern as to her ability to become pregnant. She now volunteered the information that during her eleventh year, she had been terribly upset by the death of her mother during a delivery. Next she discussed her recent nervous breakdown which she alleged had increased her menstrual discomfort, and had driven away her lover who feared that she was going crazy.

This history warrants a thorough investigation of three events: the first menstruation, the severity of the menstrual pain in her eighteenth year, and the influences which brought about the nervous breakdown. It was not possible to undertake such a comprehensive psychotherapeutic task in the clinic. However, in support of the assumption that these three stages of her neurosis are fundamentally contained in her first menstruation, is the concern about childbearing.

For this reason, the investigation was designed to elicit only a few paramount features of the nervous breakdown. She stated that she had enjoyed sexual intercourse with her lover, but, because of fear of

pregnancy for which she felt she was too young and unprepared, she had restricted intimacy to once a month. This same fear caused her to reject her lover's marriage proposal and provided him with the idea that she was losing her sanity. She reacted with a depression when she realized that her romance had been broken up.

She opened the second session with the report that her last menstruation, though somewhat painful, had been free from vomiting and fainting spells. The patient was highly grateful for this slight improvement.

She described a pleasant dream in which she had walked in her grandmother's pasture and milked the cows. In her associations she referred to her mother's tragic death from childbirth. Her mother and father had constantly quarreled, often violently, and the patient, as a child, had been under much stress when she witnessed these outbursts. She was never able to make up her mind as to which parent she should defend. After her mother's death, she had the ever-present fear that she herself might succumb to the same cause. She saw in the dream a desire to lead a peaceful life, but she thought that the memory of her mother's death might be too much for her to overcome.

During her third visit to the clinic, she announced that her menstrual pain was considerably relieved, and that she had not had urinary frequency, or any of her other former symptoms. Her guilt feelings connected with her mother's death were brought to her consciousness, and this part of her neurosis was made less forceful.

The succeeding menstrual periods were free from any symptoms, except for the experiencing of a slight pain if, at this time, she was confronted with an unpleasant situation.

From this report it is clear that the patient was strongly antagonistic toward her mother. Menstruation brought unconscious memories of the death of her mother. Suppression of the identification with her mother had prevented her from a friendly and affirmative attitude toward her own womanhood, against which she protested during each menstrual period.

CASE 2.—With the onset of her menstrual period, a colored girl, nineteen, was stricken with intense cramps which sometimes remained with her until well into the second day. For at least the first three hours and sometimes for the entire first day, she had to stay in bed. She never ate during the first day because she was afraid of vomiting. In this case, as in Case 1, some urinary discomfort was present. The gynecologic examination was negative, but the patient was disfigured and showed remnants of severe rickets. She was a highly intelligent girl, observed sharply and clearly, and was capable of judging quickly and astutely.

She vividly described her first menstruation. "When I noticed the blood I was terribly excited because I'd never heard of such a thing. I believed I had an accident, had hurt myself, and the bleeding would never stop. If I urinated, the bleeding increased. I noticed that my dress was stained and I believed that I had sat down in some dye or, perhaps, I had swallowed some glass. Finally I confided in my mother who told me it will come every month. I was dreadfully scared."

The girl was profoundly resentful of the mother's attempts to dominate her life and the lives of her four sisters. She despised her mother for constantly reproaching the father, who, as the result of an accident,

was a helpless invalid. The girl wanted to leave this sad environment, but she was handicapped by her disfigurement.

She was shown how her hatred for her mother had influenced her attitude toward life. This hostility may have deprived her of the possibility of objectively considering plans for her own future. The strong emotion may have been turned against herself as happens frequently in such cases. For instance, in her determination to differentiate herself completely from her mother, she bitterly hated any resemblance she had to the parent. Such a protest, if connected with the menstruation, may call forth all of her menstrual difficulty.

When these thoughts were presented to the girl, she confirmed their correctness by revealing many additional anamnestic details to those she had already given. She stated that she had never been aware of the menstruation of her older sisters, and it was as though she had been in dread of knowing about this phase of a girl's life. On the other hand, she had been cognizant of her mother's menstruation, and this was another proof of her hostility toward the mother whose menstrual flow was, to the girl, another expression of the woman's abominableness.

In both cases presented, urinary frequency was manifested, and though in the second case it seemed less severe, it harassed the patient considerably and therefore needs some discussion. She was asked about her toilet-training. Until the eighth year, she had been a bed-wetter and for this reason, her mother had taken her to various physicians until one of them said that the enuresis was merely a mischievous deed. The mother then felt obliged to punish the little girl who consequently felt ashamed and disgraced in the eyes of her neighborhood playmates. When menstruation came, she was unconsciously reminded of her earlier lack of urinary control. (A similar psychology is discernible in the first case, the link being masturbation.)

In the menstruation which followed this revealing session, the patient was almost free from discomfort, had no pain, was active and ate normally, but in a mild degree her urinary distress remained. The next menstrual period, however, was entirely without disorder.

Unfortunately, patients who are subjected to psychotherapy at a clinic tend to be uncooperative when it comes to follow-up studies. Only a small number consults us if a relapse occurs. Almost invariably, they dislike to contact us if they have been cured. To many of them, psychotherapy is a magic procedure, especially if, after a few sessions, a symptom which has been with them for a long time, disappears. They are fearful unless further contact with the physician may jeopardize the achievement they have attained.

These two cases have shown a psychology which is typical of that encountered in a large proportion of dysmenorrheic girls. Greatest stress should be put on the first menstrual period, especially if the girl considered it a peril. The reactive panic contains some elements which can be elicited in other features of the same patient's neurosis. Menstruation becomes the realization of old guilt feelings, evidence that old apprehensions are becoming true and substantial. Most of these guilt feelings are directed toward the mother, against whom the adolescent girl may have exhibited aggressive, hostile, or unfriendly thoughts. Therefore, these conceptions are based on suppressed material. Enlightenment only penetrates the upper layer of the mind and can never

reach the depths where the repressions are harbored. For that reason instruction, as well as the patient's own experience remains almost ineffective. It is true that the reality of the following menstruation diminishes the fears experienced with the first one, but the guilt feelings are apt to create another outlet.

In the first patient, frigidity was present. The patient professed to enjoy intercourse, but practiced it only once a month. In her report the connection between her dysmenorrhea and frigidity is obvious and needs no further correlation. As her dream and the first association to it show, every pleasure is overshadowed by her thoughts about her mother's terrible fate. A similar connection can be seen in the history of another patient.

CASE 3.—A woman of twenty-five, with a history of two operations,⁹ complained about typical hysterical symptoms, including dysmenorrhea and frigidity. About the latter she was extremely concerned. Her primary dysmenorrhea was rather mild, and was replaced by some discomfort in the scar after oophorectomy. At the same site, sensations akin to vaginismus were experienced during intercourse. For the three menstruations preceding psychotherapy, menstrual pain had reappeared, increasing in intensity with each successive period.

The insecurity of her first marriage was carried over into the second and had influenced her feeling for her second husband to whom she was deeply devoted. When she experienced her first orgasm after one year of married life, her dysmenorrhea reappeared.

A dream recalled a sexual trauma which had occurred at the age of six and after I told her the trauma was the cause of her hysterical symptoms, they ceased. On the other hand, she expressed a strong resistance to the primary probing, a common reaction in neurotics. Dysmenorrhea was one manifestation of her resistance. Though reassured that even a temporary increase in the intensity of cramps should not cause alarm, the patient, nevertheless, consulted her family physician who referred her to the hospital where a presacral sympathectomy was performed. Following the operation, the patient experienced more excruciating pains than before. She decided to return for a continuation of psychotherapy.

Further psychologic study found that both dysmenorrhea and frigidity had their origin in a trauma caused by a sexual assault upon the patient in her sixth year. In marriage, orgasms were repressed in order to shut out the memory of this occurrence and the very same mechanism was responsible for dysmenorrheic cramps.

The preceding report touches upon the rather typical connection often observed between dysmenorrhea and frigidity.

Some dysmenorrheic patients discuss their frigidity without false modesty, while others shy away from the subject. The relation between dysmenorrhea and other neurotic symptoms must be investigated and qualified, otherwise the diagnostic means are not exhausted.

A similar result of the sympathectomy, in the author's experience, is rather common in neurotic patients. Extirpation of a relatively small number of nerve fibers is unlikely to sever all connections between the

uterus and the central nervous system. The psychic effect of this operation is tremendous; therefore, a psychologic examination of patients whose dysmenorrhea was cured by sympathectomy may throw some light upon this mechanism.

Pathologic Menopause

The neurotic features of a dysmenorrhea shape the manifestations of the pathologic menopause. This period is influenced by almost every disease which an individual had during life, complicated by both endocrine and psychic characteristics. E. Bleuler³ stresses the similarity between the symptoms of puberty and those of the menopause. If a patient's reaction to her first menstruation or to the appearance of the earliest signs of puberty is examined, it will be found that there is much in common between the two. This may explain the variety of climacteric disorders.

CASE 4.—The history of a white woman, married and forty years of age, seeking relief from menopausal symptoms, is complicated by attacks of asthma. Five months prior to consultation, the patient was subjected to x-ray castration for fibroids and hemorrhages. Asthma bronchiale was twice manifested, the first series of attacks occurred during the delivery of her first child and was cured by a visit to her native country. Ten years later, after her second pregnancy, her asthmatic attacks recurred. Medical care relieved her of this symptom for a time.

About one month after irradiation, these attacks reappeared again together with her first "hot flushes," dizziness, vomiting, and feeling of emptiness in the head which augmented her climacteric symptoms. Stilbestrol controlled these attacks, but its use seemed contraindicated by the patient's tendency to bleed. She had suffered from a tuberculous pleurisy combined with pneumothorax when she was sixteen. Attacks of asthma regularly followed dreams or quarrels with her husband and children.

The patient's description of her marriage portrayed an incessantly frustrated woman. She married at twenty-four, became pregnant immediately and showed much concern about her husband's devotion, of which she had felt insecure due to the change in her appearance because of pregnancy. When her asthma was manifested, her husband left no stone unturned to help her; he had consulted numerous physicians and had sent her to different spas. Finally, her native country relieved her from this symptom.

The patient's sexual feelings became moody. For some time she did not experience any orgasm, but for some unknown reason, it came back and was strong again. After the second confinement, fear of another pregnancy dominated her to the extent that she hardly consented to intercourse. After the x-ray castration, the patient became aware of a kind of defectiveness, and that sensation made her hypersensitive and so irritable that she had constant quarrels with her family.

She had suffered with severe menstrual symptoms from her menarche at the age of fifteen. At that time she was exposed to great hardships. Because her native country was at war, she had to move, was devoid of the slightest comfort of living. When she had noticed her first period,

she went through an ordeal of fears and apprehensions. She depicted a state of dyspnea which she had experienced at that time, and which she believed was due to menace of the war. Dreams showed the source of these dyspneic attacks. She was never enlightened about sexuality, and was never conscious of the difference between the sexes. At the age of twelve, a cretin exhibited his genitals to her, and the patient believed she was about to get the same organs. This occurred at a time when she was alarmed by the pubertal changes of her body. This experience was forgotten, but revived with her first menstruation. This apprehension was kept alive for a long time and regularly induced dyspneic attacks. After she had manifested the tuberculous symptoms, the character of her dyspnea was changed and the latter disappeared completely after cure of the pleural symptoms.

When the patient was first seen, she was conscious of the fact that asthma and climacteric manifestations substituted for each other. When she experienced flushes, the asthma subsided and vice versa.

During treatment, the patient brought forth another interesting dependency; she was able to alleviate her menopausal symptoms by an enema. This fact led to the investigation of her conceptions about pregnancy which the patient had never ceased to fear. The growth of her fibroid and the subsequent bleeding irregularities gave her much trouble, once in favor of pregnancy and on the other hand refuting it. All these emotions were transformed into a deep hatred of her husband who enjoyed relations with her despite her troubles. She became extremely hostile to him, but was ashamed of these feelings.

When these dependencies were elucidated, the patient's symptoms subsided. The noxious principles of her puberty seemed to lose their hold upon her; follow-up showed that she had acquired a well-integrated personality. For the last two years she did not experience a single attack of asthma, and her other symptoms, although present to a slight degree, did not concern the patient.

The individual features peculiar to each clinical picture will reveal the factors responsible for the symptom in question. The clinical picture of every woman passing through the climacteric depends on three components: (1) the patient's constitution; (2) the residuals of her former illnesses; and (3) the neurotic trends, one expression of which may be dysmenorrhea plus its transformations and variations. In every case it is incumbent upon the physician to determine how far and to what extent a neurosis may affect the climacteric features.

Suggestions for Treatment

Having described several concomitants and corollaries of functional dysmenorrhea, some suggestions may be appropriate concerning the management and treatment of this symptom in patients whose psychologic conflicts are of a superficial character. Some women feel that menstrual discomfort is dependent upon their frame of mind. Whether false or true, such a statement may be helpful in approaching the psychic cause in a particular case.

The preliminaries do not differ from any routine examination. The physician listens attentively to the patient's descriptions of her men-

strual ailment and even encourages her to bring out details. Every comparison made by the patient is significant; for example, should she associate cramps with confinement, this would be a cue to her strong preoccupation with this subject in one way or another. The statement, "I feel so irritable, I would like to jump out of my skin," may be a protest against womanhood. A childless woman, by this same statement, expresses her resentment of her sterility, while in another patient menstruation may remind her of a miscarriage which she had suffered, and she gives expression to her grief through such articulation.

By close collaboration with the patient, the physician discovers the meaning of such statements. It is never possible to apply the solution found in one patient to another. The same utterance used by different patients may have other meanings, may be related to different epochs of their lives, and directed against various persons. Nevertheless, the elucidation of one situation alone may sometimes alleviate or even cause the disappearance of the neurotic part of the symptom and, by this means, the symptom itself.

Patients suffering from secondary dysmenorrhea may be subjected to this treatment, since the reasons underlying the symptom are easily accessible. A case in point is that of a girl of nineteen who suffered from menstrual cramps and manifested dysmenorrhea six months after the onset. In the course of her examination it was revealed that, when menstruating, she had been ordered by her mother to perform a task necessitating her prolonged immersion in a cold brook. At that time, she experienced her first attack of cramps. All subsequent menstrual periods were accompanied by a burning sensation. As a result she remained in bed the first two days of her indisposition. When talking of her mother, she exhibited strong emotions of hate. She confessed that she was an illegitimate child and that this had made her life miserable. When shown in detail how her own feelings had influenced her and had prevented her from attaining contentment in life, the patient realized the explanation. The advent of favorable circumstances, being courted, and improved prospects as to employment, brought about a change in her neurotic attitude. These elements were used to adjust the patient to reality and help detach her from her neurotic dysmenorrhea, evidently a consequence of the fixed preoccupation with her unhappy past and the numerous disappointments of her childhood.

When dysmenorrhea is manifested only after an abortion, the abortion may be the cause. Regret and sorrow at the loss of the child, or a need for self-punishment, may produce this symptom. The same may be true of a frustrated love affair, or marital discord. Nongenital ailments may also produce this symptom.

Conclusions

It is impossible to describe all neurotic concomitants of dysmenorrhea in the close compass of this paper. This syndrome, like "every medical

problem, includes a psychologic component," M. D. Mayer.⁶ It warrants earnest study and a most thorough examination. The consideration of one factor as the only etiologic principle remains fragmentary; the honest researcher is uneasy until he has considered all sides of this baffling question. The evaluation of the whole personality is achieved, if we regard both the organic and the psychic makeup of the patient.

The importance of the symptom diagnosed as dysmenorrhea has been underestimated even in the psychiatric literature. If we direct our attention to all its features, it is not as changeable as is generally assumed. To use a comparison, it behaves like an iceberg, whose bulk is submerged, leaving only a very small part of the mass visible. It must be stressed again that the majority of sufferers prefer to retain the symptom of pain, especially if it is not too severe. This apparently masochistic trait is one of the many peculiarities, common to many a neurotic feature, but intelligible to those who have some insight into the nature of neuroses.

In this paper only a partial description of the psychologic aspect is given, and many readers, therefore, may find their observations somewhat at variance with those described here. The protean exterior of the symptom, the underlying causes of which are not yet obvious, but hypothetical, presents itself differently to each investigator. The neurotic patient shows to each observer another facet of this polymorphic structure.

Summary

1. As a psychosomatic entity, dysmenorrhea is understandable, if the psychic mechanism can be explained by carefully elucidating the history. The psychogenesis is coordinated to the neurosis and all its symptoms.

2. A definition of this symptom is given in an effort to comprehend all its manifestations, and to relate them to the whole personality.

3. The persistence and manifestations of the underlying psychic energy are shown in two case reports; in another, the dysmenorrhea was replaced by other neurotic symptoms.

4. Psychotherapy in secondary dysmenorrhea seems promising, as demonstrated in one case report.

5. Another feature of this symptom is, in the author's opinion, the fact that its investigation provides an approach to the unconscious of neurotics in any psychotherapeutic procedure.

Acknowledgment must be made to Dr. Max Schneider who examined Cases 1, 2 and 4 and referred them for psychic treatment.

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1192 PARK AVENUE

FETAL ELECTROCARDIOGRAPHY AND STETHOGRAPHY

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THE following study consists of single observations upon 22 pregnant women in various stages of gravidity. An attempt to record a fetal electrocardiogram and stethogram was made on each subject. Three cases were discarded because of technical difficulties.

Graphic methods for the study of the fetal heart were attempted as early as 1906.^{1, 2, 12} These attempts were intermittent and largely unsuccessful because of technical difficulties. It was not until after 1930³⁻¹¹ that improved technique resulted in the registration of clearly discernible fetal electrocardiographic deflections. With the recent introduction of various amplification devices an ever increasing percentage of positive fetal electrocardiograms has been obtained.

Since the degree of amplification of fetal electrical potential determines the successful registration of fetal deflections, a greater percentage of positive tracings has been obtained with a tube amplifying apparatus than with a string galvanometer. However, with the string loosened to double or triple standard (1 millivolt to 2 or 3 cm.), the string galvanometer will yield positive tracings in a considerable number of cases.¹³⁻¹⁴ This was the method employed in our study.

Graphic registration of fetal heart sounds is a more recent development. Fetal heart sounds were recorded on phonographic discs as early as 1923.²⁵⁻²⁹ The first recorded fetal stethograms were reported in 1938.³⁰ To date, there have been few published studies of fetal stethography.³¹⁻⁴¹

Technique

The patient was placed in the dorsal position. The limb leads were discarded early in our study because of the uniformly negative results. Abdominal leads were taken by placing the limb electrodes upon the following sites: right upper quadrant paired with symphysis (RUQ-S); epigastrium paired with symphysis (E-S); left upper quadrant paired with symphysis (LUQ-S); right umbilical region paired with left umbilical region (RUR-LUR); right lower quadrant paired with left lower quadrant (RLQ-LLQ). The right arm wire was attached to the first electrode, the left arm wire was attached to the second electrode and lead one was taken. The string was adjusted for a deflection of 2 to 3 cm. for one millivolt of current.

For stethography the following technique was employed. An attempt was made to locate the point of maximum intensity of the fetal heart with an ordinary stethoscope. If detected, the microphone was placed over that site and held in place by a rubber belt. In cases where no fetal heart sounds were audible, the microphone was placed in each of the four quadrants.

Material

The subjects used were picked at random from the ante-partum clinic of the Bronx Hospital. The gravidity of the patients varied from 5 months to just before term.

Electrocardiographic Findings

Of the 19 cases studied, nine showed easily discernible fetal deflections occurring at regular intervals. One case showed occasional irregularly spaced fetal deflections and 9 cases failed to record any deflections in any of the leads. Percentage of positive records is 53. In our study it would appear that fewer positive tracings are obtained in the seventh and eighth months than in fifth, sixth, and ninth months. Only 2 cases out of 8 in the seventh and eighth months were positive whereas 8 cases out of 10 showed fetal deflections in the fifth, sixth, and ninth months.

TABLE I. GRAVIDITY

| Months gravid | 5 | 6 | 7 | 8 | 9 |
|-----------------------------|---|---|---|---|---|
| Number of cases | 3 | 3 | 3 | 5 | 4 |
| Number of positive tracings | 3 | 2 | 1 | 1 | 3 |

Inasmuch as previous studies not included in this analysis failed to reveal any fetal deflections under five months' gravidity, such cases were omitted from this study.

TABLE II. WEIGHT OF MOTHER

| Weight (in pounds) | 120 to 140 | 140 to 160 | Over 160 |
|-----------------------------|------------|------------|----------|
| Number of cases | 8 | 7 | 4 |
| Number of positive tracings | 4 | 5 | 1 |

The age of the mother and her parity had no bearing on the incidence of positive fetal electrocardiograms. Similarly, the presentation of the fetus and its sex were not determining factors in the obtainment of positive tracings. The weight of the mother appeared as a factor in the incidence of positive tracings, the greatest number having been obtained in the weight group of 140 to 160. It is reasonable to suppose that the weight of the fetus at the time the record is taken (not its birth weight) is a factor.

TABLE III. LEADS SHOWING NUMBER WITH POSITIVE FETAL DEFLECTIONS

| RUQ-S | E-S | LUQ-S | RUQ-LUQ | RUR-LUR | RLQ-LLQ |
|-------|-----|-------|---------|---------|---------|
| 5 | 6 | 6 | 0 | 1 | 2 |

This demonstrates that the best leads were those connecting the fundus uteri to the symphysis pubis. We previously noted that the mothers' limb leads were uniformly unsuccessful and were therefore discarded.

TABLE IV. TYPES OF FETAL DEFLECTIONS

| | SINGLE UPWARD DEFLECTIONS | SINGLE DOWNWARD DEFLECTIONS | DIPHASIC DEFLECTIONS |
|--------------------|---------------------------|-----------------------------|----------------------|
| Number of Patients | 1 | 6 | 3 |

It has been noted by other investigators that a downward fetal deflection is indicative of vertex presentation, and an upward deflection

denotes a breech presentation. All of our positive cases were delivered as vertex presentations. The one case of upward deflection in our series was taken at six months' gravidity. At that period of gestation the presentation is not fixed, and consequently, it may have been a breech which rotated spontaneously to vertex at term.

Amplitude.—The amplitude of the deflections ranged from $\frac{1}{4}$ mm. to 3 millimeter. It is interesting to note that the three cases with the largest deflections were diphasic.

Rate.—The fetal rates varied from 125 to 150. No relationship between the fetal rate and the sex of the fetus was noted in this study. The rhythm was regular in all but one. The latter showed sinus arrhythmia.

Fetal Stethography.—Of the 19 cases studied, successful fetal stethograms, with both heart sounds, were recorded in 13 instances; one sound

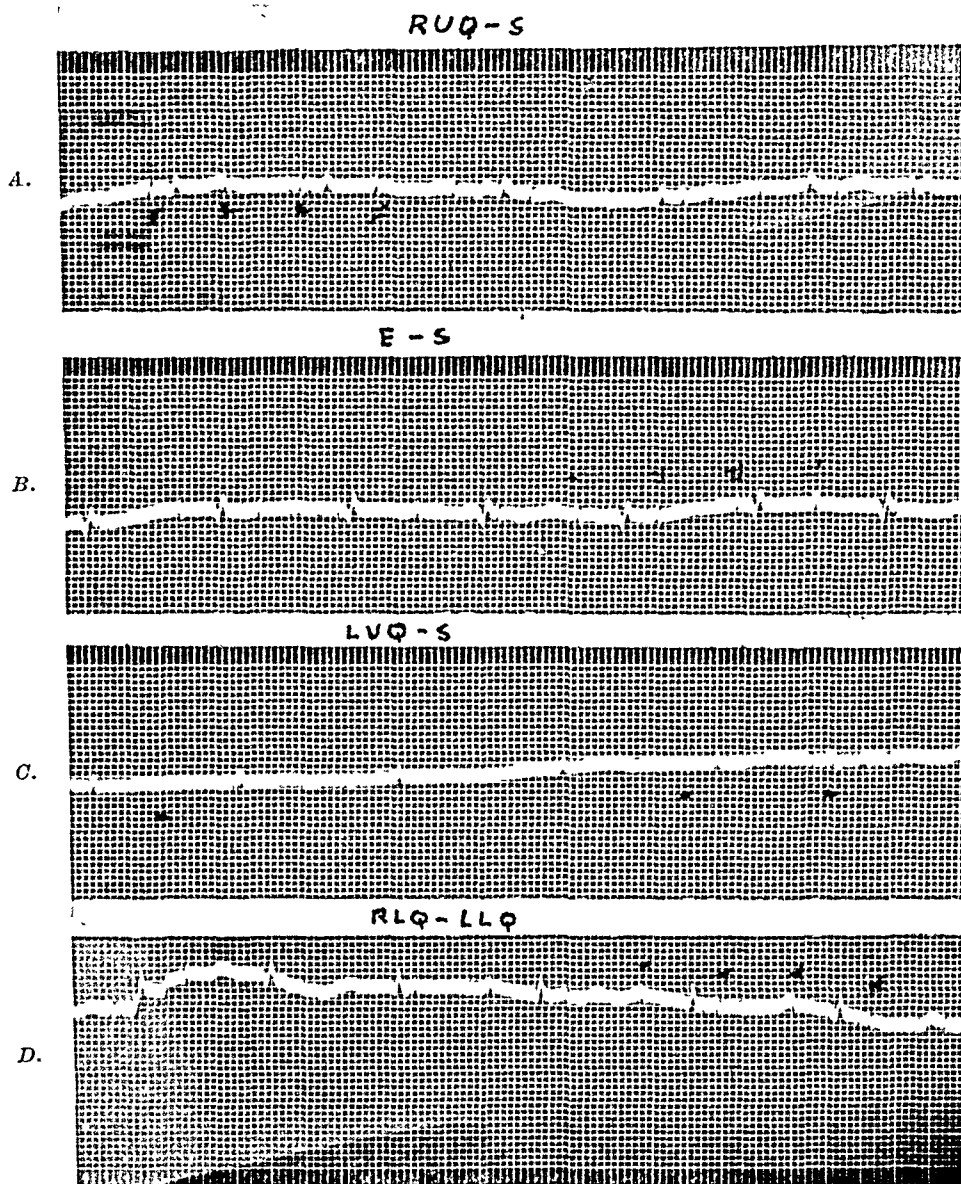


Fig. 1.—Case No. 10. Six months gravid. A, abdominal lead, right upper quadrant to symphysis; B, abdominal lead, epigastrium to symphysis; C, abdominal lead, left upper quadrant to symphysis; D, abdominal lead, right lower quadrant to left lower quadrant; E, fetal electrocardiographic deflections.

only in two cases. In four cases no stethograms were obtained. No attempt was made to measure the amplitude of the sound deflection because the latter could be varied at will by varying the magnification of the recording instrument. The number of deflections making up the first sound varied from 2 to 6; the number of deflections making up the second sound varied from 2 to 4. In most instances both first and second sounds were made up of 3 deflections. The duration of the first sound varied from 0.03 to 0.06 second. The duration of the second sound varied from 0.03 to 0.05 second. The first sound was longer than the second sound in 6 cases and equal to it in 6 cases. In only one instance was the second sound longer than the first.

Practically all of the first and second sounds assumed one of three patterns resembling M, N, or W.

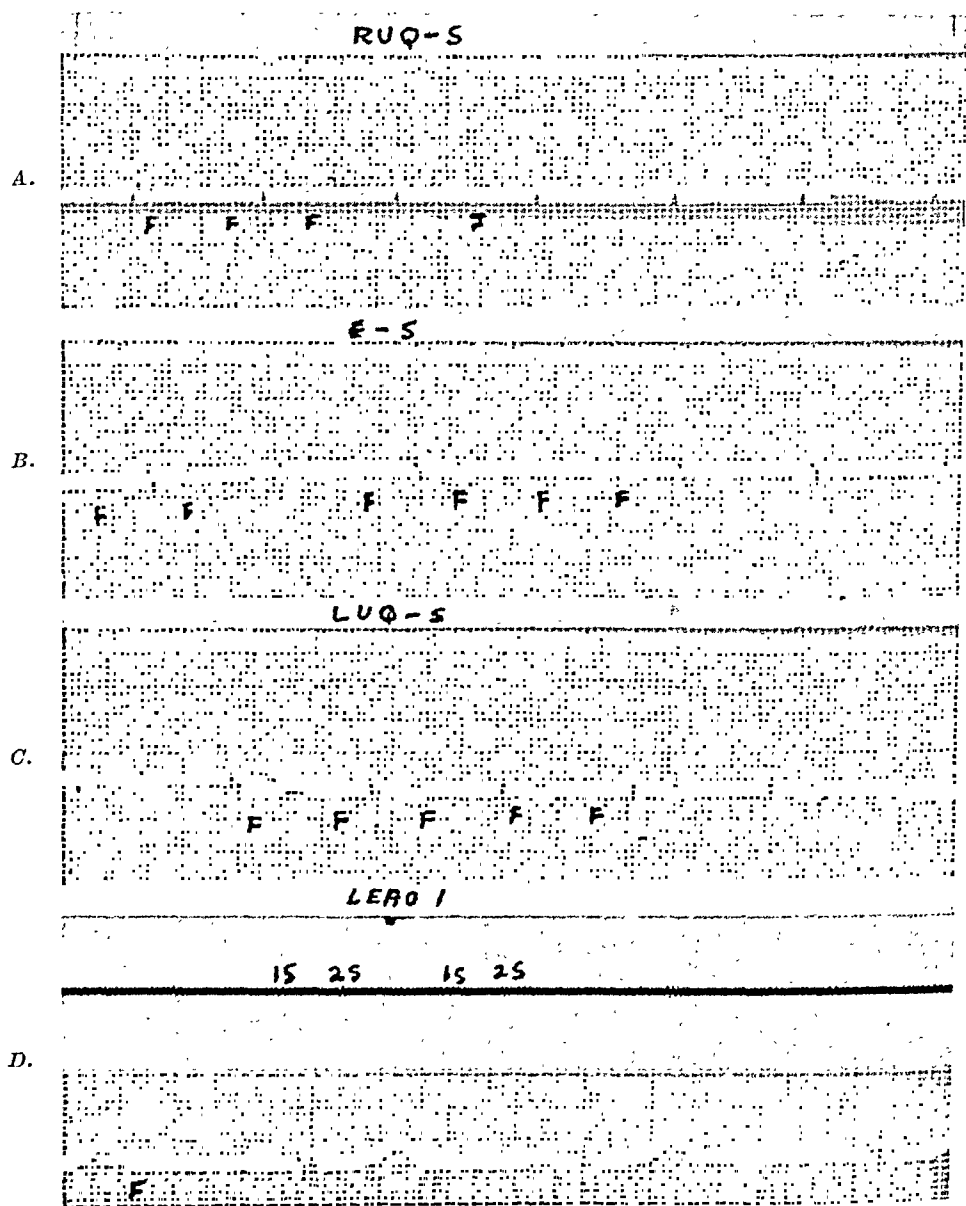


Fig. 2.—Case No. 23. Nine months gravid. A, Abdominal lead, right upper quadrant to symphysis; B, abdominal lead, epigastrium to symphysis; C, abdominal lead, left upper quadrant to symphysis; D, fetal stethogram, mother's electrocardiogram; F, fetal electrocardiographic deflection; 1S, first fetal heart sound; 2S, second fetal heart sound.

The duration of systole was shorter than diastole except in two cases in which they were equal. The duration, of course, depended upon the fetal heart rate and varied from 0.18 to 0.20 for systole and from 0.20 to 0.30 for diastole.

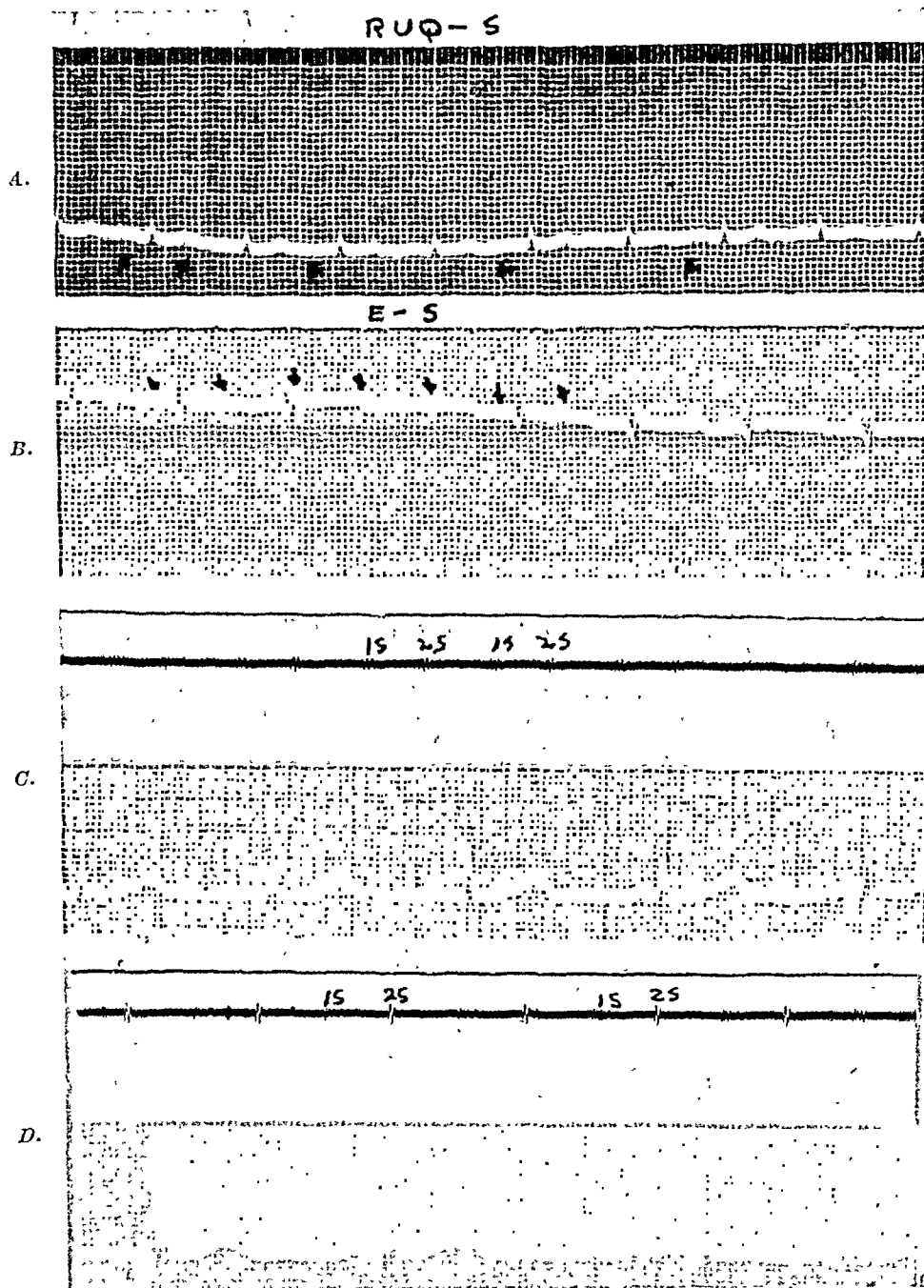


Fig. 3.—A, Case No. 13, 5 months gravid, fetal electrocardiogram; B, Case No. 20, 7 months gravid, fetal electrocardiogram; C, Case No. 15, 9 months gravid, fetal stethogram; D, Case No. 11, 5 months gravid, fetal stethogram; E, fetal electrocardiographic deflection; 1S, first fetal heart sound; 2S, second fetal heart sound.

Discussion

The result of our study has confirmed the observations of other investigators in the field. Positive fetal electrocardiograms are obtained

in a large percentage of cases even with a technique which is still imperfect. It is obvious now that with improved technique, particularly with regard to amplification, 100 per cent is not unlikely.

When this point is achieved, the practical value of fetal electrocardiography and stethography will be unquestioned. Viability of the fetus, pseudocyesis, multiple pregnancies, fetal arrhythmias and fetal distress will be diagnosed or confirmed by graphic methods. Perhaps even the subject of congenital cardiac lesions may come within the scope of these procedures.

It is of interest to note that there were less positive tracings obtained in the seventh and eighth months of gestation than in the fifth, sixth, and ninth. This is in accord with the findings of other observers. A possible explanation for this phenomenon is the relative increase of amniotic fluid during those two months. The weight of the mother, as well as the size of the fetus at the time of recording are apparently also factors in determining the production of fetal deflections.

An analysis of the fetal stethograms reveals that the concept of embryocardia is false in its implication. Embryocardia is commonly understood to mean equidistant heart sounds of equal intensity, quality and duration. This study proves that the fetal heart sounds differ from each other in a manner similar to those of the adult sounds. The first and second sounds are never identical in appearance in the same fetus. Similarly, diastole is longer than systole and approaches the latter in rapid rates.

Summary and Conclusions

1. An attempt was made to record fetal electrocardiograms and stethograms in 21 gravid women of varying periods of gestation.
2. Positive fetal electrocardiograms were obtained in 53 per cent.
3. Positive stethograms were obtained in 79 per cent.
4. Where large fetal electrocardiographic deflections were obtained they were diphasic, otherwise they were single downward spikes in all but one case. The latter was probably a breech presentation at the time the record was made.
5. The weight of the mother and size of the fetus influence the successful demonstration of the fetal electrocardiogram.
6. The age of the mother, her parity, fetal presentation and fetal sex are not factors in determining the production of fetal electrocardiographic deflections.
7. The fetal cardiac rate bears no relationship to its sex.
8. Limb leads are of no value in obtaining fetal electrocardiograms.
9. The best abdominal leads were those connecting the fundus of the uterus with the symphysis pubis.
10. The pattern of a fetal stethogram resembles that of the adult.
11. The configuration of the sounds assumes the form of M, N, or W.
12. The term embryocardia is a misconception.

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THROMBOCYTOPENIC PURPURA IN PREGNANCY

Review of the Literature With a Report of Three Cases

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PURPURA hemorrhagica is at best a rare disease, but its coexistence with pregnancy is rarer still. Hence, the admission of a Negress five months pregnant, who developed purpura hemorrhagica led to the review of the literature which follows. We shall consider purpura, first in general, and then its relationship to pregnancy.

Purpura is so inclusive a term that it is well to use Wintrobe and Rosenthal's classification, which is as follows:

- I. Primary, Essential or Idiopathic
 1. Acute
 2. Chronic
- II. Secondary or Symptomatic
 1. Blood diseases
 - (a) Anemia, aplastic, hemolytic or caused by metastases to the bone marrow
 - (b) Leucemia
 - (c) Splenomegaly, Banti's disease or Gaucher's disease
 2. Infections, acute or chronic
 - (a) Septicemia
 - (b) Subacute bacterial endocarditis
 - (c) Typhoid fever
 - (d) Scarlet fever
 - (e) Syphilis
 - (f) Tuberculosis
 3. Intoxications
 - (a) Quinine
 - (b) Benzol
 - (c) Snake venom
 - (d) Sulfonamides
 - (e) Ergot
 - (f) Arsenicals
 - (g) Mercuric bichloride
 - (h) Gold salts
 - (i) Belladonna
 4. Radiation
 - (a) Radium
 - (b) X-rays
 5. Jaundice
 - (a) Hepatitis
 - (b) Cirrhosis
 6. Chronic nephritis with nitrogenous retention
 7. Food sensitivity (Orris root, etc.)
 8. Vitamin deficiency (C, P and K)
- III. Congenital

Symptomatic purpura while usually nonthrombocytopenic, may occasionally be thrombocytopenic, e.g., following arsenical treatment or exposure to x-ray. Though most of the cases which occur in pregnancy are of the symptomatic variety, we will confine our discussion to the primary type of thrombocytopenic purpura.

Purpura was first observed in pregnancy by Arand in 1765. Ten years later, in 1775, Werlhof described essential purpura for the first time. Almost a century elapsed till Barnes reported what is commonly considered the first case of purpura in pregnancy. In 1887, Denys first noted the absence of platelets in purpura and subdivided purpura into two types, thrombocytopenic and nonthrombocytopenic. Hayem, in 1896, discovered that patients with thrombocytopenic purpura had poor clot retraction. In 1911, Duke demonstrated that while the bleeding time was increased, the clotting time was normal. In 1916, Schloffer of Prague, at the insistence of Kaznelson, performed the first successful splenectomy for thrombocytopenic purpura. From 1920 to 1940, some 300 splenectomies have been done. Since that time, progress has been made in distinguishing essential from symptomatic purpura; in observing the effect of splenectomy and in experimenting with innumerable medical treatments.

Thrombocytopenic purpura is more common in women than in men. It usually makes its appearance in the first decade of life, or in the adolescence. In one series, 70 per cent of the patients were less than 24 years old, while in another 27 per cent of the patients were girls less than ten years of age. It is stated that under the age of ten and over 40, it is a mild disease with remissions. It is thought to be rare in the Negro, but in one series of 43 cases reported by Limarzi, there were three Negresses.

Theories concerning etiology are many, but they resolve themselves into two main types: (1) Defective production of platelets in the bone marrow; or (2) increased destruction of platelets by the spleen. Limarzi champions the former theory, stating that thrombocytopenic purpura is due to faulty maturation of the megakaryocytes in the bone marrow, and that splenectomy cures the disease by removing a factor which is inhibitory to their proper maturation. Frank and Kaznelson hold to the latter opinion. Frank believes that the spleen produces a myelotoxic substance, which by causing a decreased production of megakaryocytes, results in fewer platelets. Kaznelson also believes that thrombocytopenic purpura is due to thrombolytic activity of the spleen. He adduces the following evidence: (1) Megakaryocytes are present in the blood and bone marrow in normal amounts prior to splenectomy and, (2) platelets increase after splenectomy. A thrombolytic substance has been postulated by some investigators. In 1938, Troland and Lee reported that intravenous injection of acetone extracts of spleens removed from patients with thrombocytopenic purpura reduces the number of platelets in the circulating blood of rabbits. There

is a rapid fall in the platelets, and an even sharper return to normal in 48 hours. Despite the fall in the platelets, there are no hemorrhagic manifestations. Jerome similarly reported a transient significant depression in the platelet count, but not on the bone marrow or the megakaryocytes. Other observers, such as Paul and Uihlein, have failed to demonstrate, or disprove the existence of such thrombocytolytic substances.

Platelets are formed by budding from the cytoplasm of the megakaryocytes in the bone marrow. They are spheric or ovoid, granular bodies about two to four microns in diameter with a life expectancy of three to five days. By producing thromboplastin, they initiate clotting. The normal number in the blood is 200,000 to 400,000/cubic millimeters. Forty thousand is regarded as the hemorrhage level. After a splenectomy, the level of platelets rises to normal in 24 to 48 hours. From then on it may be supernormal, or may fall slightly below normal. Thrombocytopenic purpura is believed by Whitby and Britton to be due to (1) quantitative deficiency of the platelets caused either by primary defect of platelet formation, or pathologic destruction in the spleen or, (2) qualitative deficiency of the platelets. It is not due to the small number of platelets because patients with low platelet counts may not bleed. Further, the bleeding is not due to the increased bleeding time because this is not invariably present. Though there is no convincing evidence that it is due to the capillary bed, Brill and Rosenthal feel that the changes in the platelets cause changes in the capillary walls, while McFarlane states that in thrombocytopenic purpura the capillaries have malformed loops, damaged endothelium and defective contractility. So, at present, there is no adequate explanation as to why patients with thrombocytopenic purpura bleed.

Yet, despite this lack of explanation, bleeding is the chief symptom of thrombocytopenic purpura. The patient usually comes to the doctor complaining of bleeding from the mouth, or epistaxis, or hematuria. The acute phase is more common in early life and the patient may progress to death from anemia or intracranial hemorrhage. This latter is the most feared complication and may result in hemiplegia, meningitis or death. Recovery from the acute attack occurs in two weeks to several months. From then on the disease may be chronic with remissions and exacerbations.

The most striking physical sign is the presence of purpuric spots varying in size from the point of a pen to the head of a pin. They may even increase in size until they become ecchymoses. Clotted blood may be seen at the nares, or the gum margins. Infection of the mouth, with Vincent's organisms is a common association. The liver and spleen are rarely enlarged. Most authorities agree that the spleen is palpable in less than one-third of the patients with thrombocytopenic purpura and further state that if the spleen is enlarged, the disease is more likely a symptomatic purpura.

The diagnosis is confirmed by the platelet count. This is the only constant laboratory feature. Whereas the platelets are normally 200,000 to 400,000/cu. mm., they are less than 100,000 and may even be absent. The second most important laboratory measure is aspiration of the sternal bone marrow. Normally mature megakaryocytes are present, while in thrombocytopenic purpura the bone marrow is normal, or there is a megakaryocytic hyperplasia. Some authors state that there exists a uniform stimulation of all the elements of the bone marrow with myeloid, erythroid and megakaryocytic hyperplasia. Immature megakaryocytes with hyalinization and vacuolization of the cytoplasm, and degenerative types of nuclei are seen. This test excludes metastases, aplastic anemia and the leucopenic phases of leucemia. Prolongation of the bleeding time is the third distinguishing characteristic. By Duke's method, this is normally one to three minutes. It may in thrombocytopenic purpura, however, be prolonged from ten to ninety minutes or strangely enough, may be normal. Clot retraction normally begins in one to two hours and is complete in 18 to 24 hours, while in thrombocytopenic purpura a soft clot forms which often shows no tendency to retract in 48 hours. In thrombocytopenic purpura petechia usually occur after the Rumpel-Leede test, the so-called capillary resistance test, whereas normally they do not. The clotting time, which by the Boyce-McFettridge technique is normally 8 to 10 minutes, is normal. The white blood count may be normal, or there may be a leucocytosis. The degree of anemia is proportionate to the blood loss. Blood levels for calcium, fibrinogen, vitamin C and prothrombin are normal.

Thrombocytopenic purpura must be distinguished from a host of diseases. The chief of these, symptomatic purpura of the nonthrombocytopenic variety, whether due to allergy, infection or idiosyncrasy to food or drug, is readily distinguished by its normal platelet count, normal bleeding time and the presence of clot retraction. Hemophilia is differentiated because there is usually a familial history which does not exist in thrombocytopenic purpura; the bleeding in hemophilia is caused by trauma; the bleeding time is normal, the clot retraction and the platelet count are normal while the clotting time is prolonged. Thrombocytopenic purpura is readily distinguished by laboratory data from acute aplastic anemia in which there is deficiency of all the formed elements of the blood, and from acute leucemia in which immature white blood cells are present in the bone marrow and the blood smear. Lack of vitamin C, commonly called scurvy, and deficiency of vitamin K may be readily excluded by obtaining blood levels for the respective vitamins. A few rarer diseases, such as familial epistaxis, hereditary hemorrhagic telangiectasia, polycythemia vera, lupus erythematosus disseminatus, von Willebrand's thrombopathy or Glanzmann's hemorrhagic thrombasthenia are distinguished by the absence of the blood findings characteristic of thrombocytopenic purpura.

TABLE I. CRITERIA FOR THE DIAGNOSIS OF ESSENTIAL THROMBOCYTOPENIC PURPURA

| | NORMAL | THROMBOCYTOPENIC PURPURA |
|---|--|--|
| Platelet count | 200,000/cu. mm. 400,000/cu. mm. | Less than 100,000/cu. mm. May be entirely absent Only constant abnormality |
| Bleeding time (Duke's method) | 1 to 3 minutes | 10 to 90 minutes This may be normal |
| Capillary resistance test (Rumpel-Leede) | No petechiae | Petechiae |
| Sternal puncture | Normal | Megakaryocytic hyperplasia |
| Clot retraction | Begins in 1 hour, complete in 24 hours | May not begin in 24 hours |
| Anemia | None | Normocytic, proportionate to the bleeding |
| Clotting time (Boyce-McFettridge Method) | 10 minutes | Normal |
| Vitamin C | 0.8 to 1.2 mg. % | Normal |
| Vitamin K (Werner, Brinkhous Smith) | 100% | Normal |
| Abnormal cells in bone or blood | None | None |

Treatment

The treatment of thrombocytopenic purpura is both medical and surgical. In the acute phase, the patient is placed in bed, a high protein and high vitamin anti-anemic diet is given and Feosol is administered. In accord with the recommendations of Squire and Madison, foods to which the patient might be sensitive are eliminated from the diet. Blood, citrated and fresh, or red cell transfusions are given to control the bleeding, to keep the red cell count above 2,000,000 and to keep the blood pressure above 90. Moccasin venom, in dosage of 0.4 to 1.0 c.c. of 1 to 3,000 solution may be given subcutaneously twice weekly. This, however, is without proved effect. High voltage x-ray, ultraviolet rays, calcium, vitamin C and parathyroid extract have been given, but most authors agree that they are of little value. Within the past year citrus pectin, in dosage of 3 to 9 grams a day has been recommended by Isaacs. This checks the bleeding without affecting the platelet count. Either spontaneously or because of the above therapy, the acute phase will subside. In this interval, foci of infection are removed or splenectomy is done. Splenectomy may also be done during an acute episode which fails to respond, but here the risk is greater. The primary mortality of splenectomy in thrombocytopenic purpura varies from 5 per cent as recorded by Wiseman to 13 per cent as reported by Walton. The preoperative preparation includes multiple transfusions and the demonstration of a hyperplastic bone marrow. If the bone marrow is aplastic, splenectomy is of no value inasmuch as we are more likely dealing with an aplastic anemia, or a leucopenic leukemia rather than an essential thrombocytopenic purpura. Splenectomy is contraindicated if there is any doubt of the diagnosis, if there is a history of recent drug ingestion and, above all, if sternal puncture

fails to reveal megakaryocytes in the bone marrow. The indication for splenectomy is a recent exacerbation of thrombocytopenic purpura which has not subsided, or an acute phase which fails to respond to medical treatment. The curative value of splenectomy in thrombocytopenic purpura is dramatic. Bleeding ceases as the splenic pedicle is ligated. The platelets sharply rise to normal in 24 to 48 hours as was shown by Brown and Elliott, then reach a peak in ten days and may later show a secondary fall. Postoperative pneumonia and atelectasis are frequent because of the intimate connection of the spleen to the adjacent thorax. Sometimes, however, splenectomy fails. This is due to incorrect diagnosis, to the presence of accessory spleens, or to a hypoplastic bone marrow.

During the acute exacerbation the prognosis is guarded. However, when the patient is less than ten years or over 40, remission occurs rapidly. The presence of hematuria is reputed to be ominous because death usually follows. At autopsy, the capsules of the kidney glomeruli are found filled with blood. From our experience this seems to be an overstatement. The development of signs of intracranial injury is also alarming. Death is usually due either to the blood loss or to the brain hemorrhage. At autopsy, the only constant feature is hemorrhage, both gross and microscopic. The bone marrow may be normal, or may show megakaryocytic hyperplasia. The lymph nodes are not enlarged. The spleen, whether removed at operation or at post mortem, is rarely enlarged but is hyperplastic. Meningitis may be superimposed on intracranial hemorrhage.

Because of its rarity, little is known about thrombocytopenic purpura in relation to pregnancy. While there is no way to estimate the number of unrecorded cases, Long states that 80 cases of purpura in association with pregnancy have been reported. Burnett and Klass in December, 1943, however, could find records of only 68 cases. Forty-six of these they considered as doubtful, 18 they regarded as representing symptomatic purpura, and only four were true thrombocytopenic purpura. Then they described in detail their case which they regard as the fifth true case of thrombocytopenic purpura recorded in the literature. On an analysis of these five cases, Burnett and Klass believe that there is no causal relationship between thrombocytopenic purpura and pregnancy, but rather that thrombocytopenic purpura has periodic lapses which may coincide with pregnancy. They state that it is equally common in multiparas and primiparas, while Mosher believes that it is more common in multiparas. Burnett and Klass further state that only one out of five patients had hemorrhagic tendencies prior to the pregnancy, and that they were normal in previous pregnancies. They further believe that thrombocytopenia develops early in pregnancy while Mosher thinks that it occurs most frequently in the second half of pregnancy. Most authors agree that no hemorrhage occurs at the time of delivery, though Mosher and also Hirst state that all cases of purpura end fatally because of hemorrhage.

Perhaps the best method of learning of the relationship of thrombocytopenic purpura to pregnancy is to narrate the few cases which have been recorded. We shall first describe the five cases which Burnett and Klass accept as being true thrombocytopenic purpura, add five more from the literature, and then report in detail the three cases which have been observed at the New York Hospital. The first of the five cases accepted by Burnett and Klass was reported by Liebling in 1926. A 22-year-old primigravida, who, when first seen in the seventh month of pregnancy, complained of bleeding from the nose and gums since the fifth month. In the sixth month the platelet count was 40,000 but one month later it rose to 300,000. An 8-pound, 11-ounce baby was delivered in whom petechiae were present and whose vomitus, urine and stool were blood stained. By the fifth postpartum day, the infant's symptoms had ceased while the mother was cured two months post partum. Siegler, in 1934, reported regarding a 29-year-old para iii, gravida v who had had purpura for the past seven years, who had had a hemorrhage after a menstrual period two years ago, and who had a postpartum hemorrhage at the last delivery. There were purpuric spots over her entire body, and her platelet count was 80,000. At delivery, the blood loss was 1,500 cubic centimeters. A 10-pound, 10-ounce infant was delivered and died on the fourth postpartum day of an unstated cause. Unfortunately, no post mortem was performed. In 1935, de Saussure and Townsend described a 35-year-old Negress, para viii, gravida ix, who at term had hematemesis, vaginal bleeding and hematuria. The next day, a stillborn infant was delivered. At the time of the delivery, the mother's platelet count was 33,000 and the bleeding time 30 minutes. The platelets at the time of discharge were 144,000. The fourth case was reported in 1939 by Bernstein, Newman and Hitzig. In early pregnancy, purpura of the skin appeared; in the fifth month, vaginal bleeding and epistaxis occurred. The platelet count was 10,000, the tourniquet test was positive, and the bone marrow was normal. The patient was treated by transfusions and splenectomy at which time a hyperplastic spleen was removed. Postoperatively, the bleeding stopped and the purpura disappeared. A 1,400-gram infant, who was free of purpura was delivered and died on the eighth day of atelectasis. At post mortem, the infant's hematopoietic system was normal. In the last case, Burnett and Klass's own, a primigravida had epistaxis and petechiae in the fourteenth week of pregnancy. The platelet count was 15,000; the bleeding time, 27 minutes; the clotting time, four minutes; the tourniquet test positive and the clot retractility normal. Spontaneous remission occurred and a 3,600-gram infant, who was normal, was delivered with little blood loss.

In addition to these five cases, there are five other cases which represent thrombocytopenic purpura. Hottenstein and Klingman, in 1927, described a 30-year-old, para i, gravida ii, who had a postpartum hemorrhage with her first delivery. When she was six months pregnant, purpura of the trunk and extremities appeared. The platelet count was

25,000. Transfusions were given and a 3,320-gram infant, who was well 8 months post partum, was delivered. By the seventh postpartum day, the mother's hemoglobin had fallen to 10 per cent. A splenectomy was done with death occurring on the second postoperative day. The autopsy revealed acute endometritis and subcutaneous hemorrhage. Limarzi, in 1940, reported another case which is undoubtedly thrombocytopenic purpura. Though purpuric spots had been present for a year prior to pregnancy, bleeding from the nose and mouth did not occur until the seventh month. After several transfusions, a spontaneous delivery of a 6-pound, 8-ounce infant occurred. There was no hemorrhage; the child was normal, and a splenectomy was done one month post partum. A third case, which is not included by Burnett and Klass, is reported by Phythyon and Lartz in 1943. A 28-year-old primigravida when seven months pregnant bled from the gums, had hematuria and purpura. The bleeding time was increased; the platelets were 68,000. After three transfusions, a splenectomy was done. On the second postoperative day, a premature stillborn infant was delivered. By the twelfth postoperative day, the platelets were normal, 240,000.

Troland and Lee describe a fourth case of a 22-year-old woman who, in August, 1936, noticed bleeding from her gums. Her blood studies were normal until in December, there was some reduction in platelets. On January 27, 1937, a normal child was born, the blood loss being 150 cubic centimeters. At the time of delivery, the platelets numbered 78,000, bleeding time was 8 minutes and the tourniquet test was positive. Throughout the next two months, vaginal hemorrhage occurred until in April, a splenectomy was done. All symptoms regressed after this, and the blood studies were normal.

A fifth case culled from the literature was reported by Polowe in March, 1940. This patient was a para i, gravida ii, who had had purpura during her first pregnancy which had occurred five years ago. In the first pregnancy the infant was normal, and apart from the need for two transfusions, the pregnancy was uneventful. In the sixth month of the second pregnancy ecchymoses, epistaxis, hemoptysis and hematuria occurred. The platelet count was 60,000, the bleeding time 12 minutes, the clotting time 11 minutes and the tourniquet test was positive. In the eighth month of pregnancy, a splenectomy was done. The spleen weighed 1,060 grams and was described as a splenoma with necrosis. About a month later, a normal baby was delivered. The author asserts, "I believe this is the first case to be reported of splenectomy in pregnancy complicated by thrombocytopenic purpura hemorrhagica." However, in 1939, Bernstein, Newman and Hitzig, and in 1943, Phythyon and Lartz, reported the performance of splenectomies during pregnancy for thrombocytopenic purpura. Also in a letter in the *Journal of the American Medical Association* in May, 1944, Grossman states that Garlock performed a splenectomy "a few years ago" for thrombocytopenic

purpura occurring during pregnancy. Doubtless there are other unreported cases. Two additional cases reported by Sanford, Leslie and Crue, and Urbanski and Hutner most likely represent thrombocytopenic purpura, but the evidence is not sufficient to warrant this conclusion.

Case Reports

From September, 1932, to June 1, 1944, 43,334 patients have been delivered in the New York Hospital. Three of these had thrombocytopenic purpura.

CASE 1.—P. S., a 17-year-old Negress. Her last menstrual period was August 22, 1943, making the expected date of confinement May 29, 1944. Since 1934, at the age of seven, she had had repeated episodes of bleeding from the gums. In 1934, the platelet count was 6,400. Until 1941, she improved on rest and transfusions but at this time, after failure to improve and with decrease of the platelet count to 32,000, splenectomy was done. Her improvement was only gradual, and she had several episodes of bleeding from the gums during the first postoperative month. In the fifth month of pregnancy, in 1944, three years after the splenectomy, she again noted bleeding from gums, dizziness, fatigue and dyspnea. When examined, purpuric spots were present, and there were clots of blood about the gum margins. Smear from the mouth contained Vincent's organisms. After several transfusions of red cells, fcosol, citrus pectin and a high vitamin diet, the patient improved so much in the course of two weeks that she was followed in the antepartum clinic and the hematology clinic.

She continued in good condition on the above-mentioned routine until May 7, when bleeding from the gums again occurred. An examination of the urine revealed hematuria, hence she was readmitted. Transfusions, ferrous sulfate, citrus pectin in increasing doses were given with marked improvement for two weeks, but then an exacerbation of the disease occurred with marked bleeding from the gums, and hematuria. On June 9, 1944, a full-term spontaneous delivery of a 3,520-gram female infant occurred. Blood loss was 50 cubic centimeters. Bleeding from the gums stopped almost immediately after delivery, but blood destruction continued as indicated in the following chart. Her puerperium was marked by a low-grade fever due to intrauterine infection with *Bacillus aerogenes* and anaerobic nonhemolytic streptococcus, and a urinary tract infection caused by *Bacillus aerogenes*. Sulfonamide therapy was deemed unwise so 600,000 units of penicillin were given with good effect. The remainder of the puerperium was uncomplicated by bleeding or fever.

The female infant weighed 3,520 grams. As no signs of purpura developed, and analyses of blood and spinal fluid revealed no evidence of internal bleeding, the infant was discharged with her mother.

CASE 2.—D. C., noticed gastric hemorrhage when she was six and had profuse menses at 14 in 1930. She then showed petechiae of the arms and legs. Prior to splenectomy which was done on April 29, 1930, the platelet count was 20,000, the bleeding time was 30 minutes, and there was delay in the clot retraction. Postoperatively, the platelet count was 100,000 and the bleeding time was 10 minutes. Subsequently, there was no bleeding tendency. In the first pregnancy, in 1939, purpuric

TABLE II. LABORATORY DATA OF MOTHERS

| | ANTE PARTUM | | | | DAY OF DELIVERY | | POST PARTUM | |
|--------------------|----------------------|----------------------|----------------------|----------------------|--------------------|-------------|-------------------------|----------------------|
| | 2/2/44 | 2/14/44 | 5/8/44 | 5/15/44 | 5/26/44 | 6/9/44 | 6/12/44 | 6/19/44 |
| Hemoglobin | 5.1 grams | 11.5 grams | 11.0 grams | 13 grams | 11.0 grams | 8 grams | 6.5 grams | 11.0 grams |
| Red blood count | 2,400,000 | 4,400,000 | 4,000,000 | 5,200,000 | 4,400,000 | 2,700,000 | 2,300,000 | 3,500,000 |
| White blood count | 16,000 | | | 9,500 | 10,700 | | | 10,150 |
| Leukocyte index | 3 | | 3 | 3 | 3 | | | 1.1 |
| Volume index | 0.84 | | 0.88 | 0.91 | 0.95 | 0.97 | | 1.1 |
| Color index | 0.79 | | 0.94 | 0.86 | 0.91 | 1.03 | | 1.07 |
| Platelets | 130,000 | 460,000 | 70,000 | 220,000 | 110,000 | 140,000 | | 130,000 |
| Bleeding time | 27 minutes | 2.5 minutes | 11 minutes | 13½ minutes | 12 minutes | 10+ minutes | 6 minutes | 15 minutes |
| Clotting time | 5 minutes | 9.5 minutes | 9 minutes | 11 minutes | 11 minutes | 11 minutes | 9 minutes | 11 minutes |
| Clot retraction | 13% serum in 7 hours | 10% serum in 4 hours | None after 4 hours | 32% serum in 4 hours | None after 4 hours | | 52% serum after 4 hours | 2% after 4 hours |
| Fragility | Fair | | Poor | Poor | Very poor | | Fair | Poor |
| Tourniquet | 1 Petechia/7 minutes | None | Neg. after 7 minutes | Neg. after 7 minutes | | | Negative | Neg. after 7 minutes |
| Prothrombin | 69% | 80% | 40% | 50% | 96% | | 41% | 76% |
| Vitamin C | 0.73 mg. % | 0.45 mg. % | 0.76 mg. % | 0.34 mg. % | 0.56 mg. % | | 0.5 mg. % | 0.5 mg. % |
| Blood type | B | | | | | | | |
| Rh | Negative | | | | | | | |
| Sedimentation rate | 0.75 | | | | | | | |
| Calcium | 10.00 mg. % | | | | | | | |
| Chemistry | Normal | | | | | | | |
| Reticulocytes | | 3% | | 3% | 1.1% | | 6.2% | |

TABLE III.. LABORATORY DATA OF INFANTS

| | 6/10/44 BIRTH | 6/13/44 3 DAYS | 6/19/44 9 DAYS |
|---|----------------------------|-------------------|-------------------|
| Hemoglobin | 16.5 Gm. | 14.5 Gm. | |
| Red blood cells | 7,100,000 | 3,800,000 | |
| White blood cells | 15,300 | 8,000 | |
| Platelets | 290,000 | 160,000 | 235,000 |
| Nucleated red blood cells (per 100 white cells) | 5 | 8 | |
| Prothrombin | | 88% | |
| Bleeding time | 3.5 minutes | | 1 minute |
| Clotting time | 16 minutes | 4 minutes | 4 minutes |
| Clot retraction | Almost complete in 6 hours | Normal | |

spots were present but all blood tests were normal. There were occasional nosebleeds one month prior to term, and the platelet count fell to 45,000. Blood loss at delivery was 60 cubic centimeters. The infant weighed 3,100 grams. About five hours after birth, many petechiae appeared on the infant's extremities. There was a cephalohematoma on the right parietal area. The petechiae spread until they covered the entire body. The platelet count was 120,000; the red cells numbered 5,400,000; the bleeding time was greater than 7 minutes and the clotting time was 3 minutes. The infant began to vomit blood-stained mucus. Despite many transfusions, the infant died on the third day. The autopsy revealed jaundice, subaponeurotic hemorrhage of the head, subarachnoid hemorrhage, hemorrhage into the subcutaneous tissue, and petechiae of the thymus and visceral pleura. In 1941, a spontaneous abortion occurred at 3 months. In the third pregnancy, in 1942 to 1943, when three months pregnant, platelet count and bleeding time were normal, but the tourniquet test showed numerous petechiae. At delivery, the blood loss was 100 cubic centimeters. A 3,300-gram baby was delivered in whom purpura developed one hour after delivery, but in whom no bleeding occurred. The platelet count was 40,000; bleeding time was more than 90 minutes; clot retraction was absent and sternal aspiration showed a decreased number of megakaryocytes, and failure of production of platelets. After multiple transfusions the child improved. Six weeks after delivery no bleeding had occurred, the purpuric spots had disappeared and the bleeding time was 3 minutes. There is no further follow-up on the patient.

CASE 3.—S. A., in 1935, at 17 years of age, had an induced labor in the seventh month because of eclampsia. In the second pregnancy, in 1936, though partial premature separation of the placenta occurred, a living 1,500-gram baby was delivered. In December, 1941, the patient noticed bleeding from the gums, vaginal hemorrhage and ecchymoses. At this time, the platelet count was 10,000, bleeding time was over 30 minutes, clot retraction was defective, while the tourniquet test was positive. The bone marrow was normal. A splenectomy was done on January 8, 1941. All bleeding ceased and the platelets rose to 360,000. The postoperative course was complicated by atelectasis and bronchopneumonia of the left lower lobe. The spleen was unremarkable. In the fifth month of the third pregnancy (August, 1943), the platelets were 520,000 and the bleeding time was one minute. In January, 1944, a 3,560-gram infant was delivered, the blood loss being 450 cubic centimeters. Both infant and mother were discharged well.

Discussion

How is the child affected by the thrombocytopenic purpura of the mother? Some answer has already been given by the case reports. A great variance of opinion exists. Mosher states that 50 per cent of the infants die in utero, or after delivery. Burnett and Klass, at the other extreme, believe that if the fetus develops purpura, it is not essential thrombocytopenic purpura but is symptomatic purpura, or is due to familial platelet defect. Rushmore, in 1925, reported seven instances in which purpura was present in both mother and child. Our second case will add two more examples of this, the first baby dying of congenital thrombocytopenic purpura, the second living and also regarded as an example of congenital thrombocytopenic purpura.

Walton states that if the blood picture of the purpuric mother shows a complete remission after splenectomy, the newborn will be free from thrombocytopenic purpura. Our third case illustrates this. Wiseman, Doan and Wilson believe that while thrombocytopenic purpura is often congenital, there is no proof that it is inherited. Whiting and Barritt report a woman who had a splenectomy at the age of 14, and who 10 years later had two babies, both of whom developed purpuric spots and died within three days after delivery of intracranial hemorrhage. They assert that these cases represent congenital thrombocytopenic purpura rather than hemorrhagic disease of the newborn because of (1) the immediate spontaneous appearance of the hemorrhage, (2) the normal prothrombin level of the second baby, (3) the fact that neither infant responded to whole blood and (4) the fact that vitamin K was given antenatally and to the baby after birth. Just what the prognosis of the baby is, is difficult to state but from an analysis of the ten cases reported, it would appear better for the infant if the disease is in a chronic phase, and if a splenectomy has been done prior to the pregnancy.

TABLE IV. OUTCOME IN INFANTS

| N.Y.H. | DIED | LIVED |
|------------|---|---|
| Case 1 | 1 (Congenital thrombocytopenic purpura) | 1 (Congenital thrombocytopenic purpura) |
| Case 2 | | 1 (Normal) |
| Case 3 | | 1 (Normal) |
| Literature | | |
| Case 4 | | 1 (Bled until the fifth day) |
| Case 5 | 1 (Died on the fourth day. No autopsy obtained) | |
| Case 6 | 1 (Stillborn) | |
| Case 7 | 1 (Post splenectomy. Died on the eighth day of atelectasis and prematurity) | |
| Case 8 | | 1 (Normal) |
| Case 9 | | 1 (Normal) |
| Case 10 | | 1 (Normal) |
| Case 11 | 1 (Stillborn, postsplenectomy) | |
| Case 12 | | 1 (Normal) |
| Case 13 | | 1 (Normal) |

Summary

Thrombocytopenic purpura has been discussed both as a disease entity and in relation to obstetrics. In addition to the five cases which are regarded by Burnett and Klass as true purpura, eight more have been added—five of these from the literature, and three from the New York Hospital records.

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A STUDY OF COMMERCIALLY MANUFACTURED CATAMENIAL TAMPONS*

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PART I

IN RECENT years, there has been a very marked increase in the use of commercially manufactured tampons for the control of women's menstrual flow. The purpose of this study was to investigate various types of commercial menstrual tampons with respect to their anatomical correctness, and the protection and comfort provided to the wearers. To make the study as generally helpful as possible, many factors were considered, and a great number of women were examined before the subjects were finally selected. Women of marked pathology were excluded and those finally chosen included women of various pelvic types and engaged in diverse occupations. The study makes final report on 25 women although many more cooperated in the work. No case has been reported unless the women were tested with at least two different tampons. Some of the women were not able to cooperate fully during the entire time, although they were seen at intervals during the course of the investigation. Three of them were tested for 7 months, 2 for 5 months, and the remainder from 1 to 4 months. Of the 25 women finally included, 12 have been rechecked within a year, and not one has shown any unfavorable effect from the use of tampons. During the period of this study, one woman was operated upon for a condition which existed before she ever used tampons, 5 women became pregnant—all primiparas—of whom 3 were delivered before the conclusion of this study.

All of the women were subjected to a routine examination. Urethral and cervical smears were taken and examined, but no cases of gonorrhea were discovered. The vaginal secretions were examined for *Trichomonas vaginalis* by the hanging drop method, and all examinations were found to be negative. A study of the vaginal epithelium was undertaken. The vaginal smears revealed normal epithelial cells to be present in all. Vaginal pH was determined by B.D.H. Universal Indicator and found to range from 3.0 to 5.5.

The women were questioned as to their previous usage of tampons—whether they had experienced discomfort, as defined to mean “an awareness of the tampon within the vagina,” or “burning,” defined as “the uncomfortable sensation at the introitus” which is noted more frequently when no inserter is used, or when the inserter is used without water or other lubricant to minimize friction during insertion. Of the

*This study was made possible by a grant from The Personal Products Corporation.

9 women who had previously used tampons, 7 had used tampon No. 7, 1 tampon No. 5, and 1 tampon No. 1. Of those using tampon No. 7, 5 reported discomfort, as did the woman using tampon No. 5, and 2 reported "burning."

Of the 25 women, 16 classified their menstrual flow as "moderate," 5 "heavy," 2 "heavy at first" and 2 "scant." When an attempt was made to correlate the individual woman's estimate of the amount of flow with the number of pads or tampons used, it became obvious that the description was often inaccurate. Conclusive results could be obtained only from correlating the length of adequate protection with the actual weight of the absorbed menstrual blood within the pad or tampon.

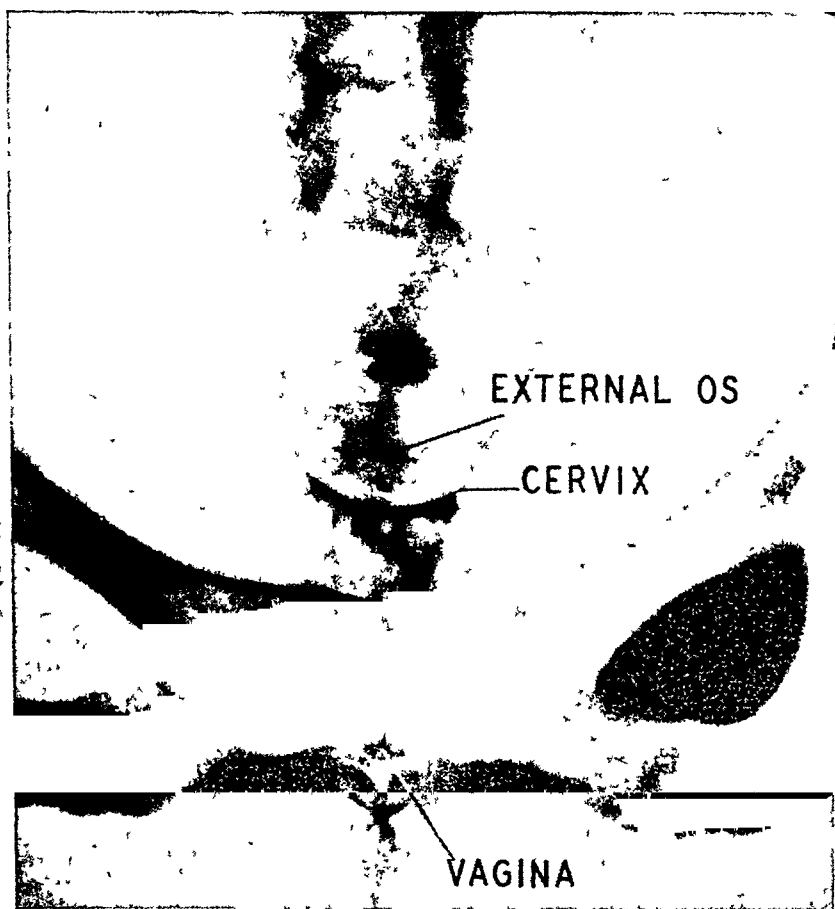


Fig. 1.—Tampon 1, after application of sodium tetraiodophenolphthalein, showing cervix and the vagina.

Studies of Commercial Tampons

Commercially manufactured catamenial tampons are of two general types. The first are those which are inserted by the user without the aid of an inserter. The other type is placed inside the vaginal tract with the aid of an inserter. Some tampons are not compressed for use, and some have been compressed to a smaller size so that they are inserted in the compressed size and expand within the vaginal canal as they absorb the menstrual flow.

The tampons numbered 1, 2, 3 and 4 in this study are those designed to be inserted without the use of a mechanical inserter.

Tampon No. 1 looks like a soft cotton ball. Its outer measurements* are $1\frac{1}{8}$ inches by $1\frac{1}{8}$ inches by $1\frac{1}{8}$ inches, and it consists of two loosely, spirally wound cotton balls separated by 8 layers of surgical gauze. The whole is fastened to

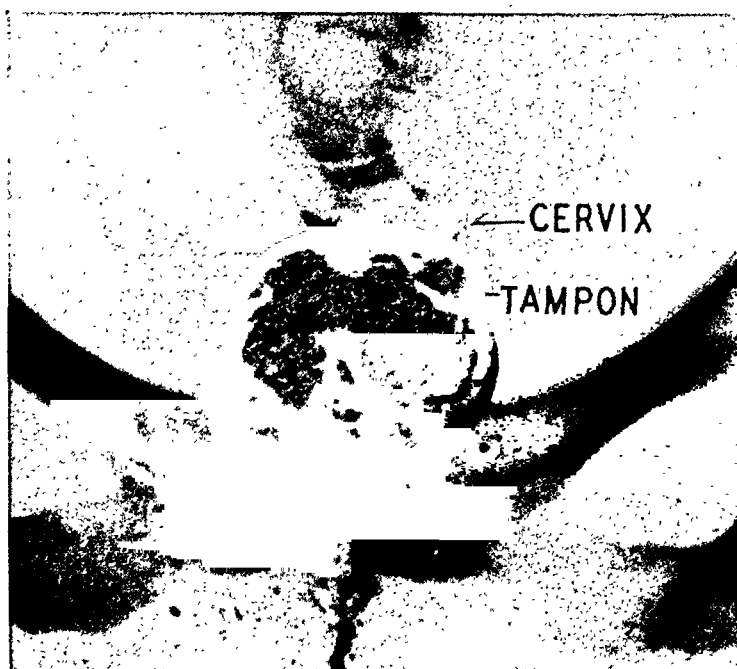


Fig. 2.—Tampon 1, showing tampon in position after insertion.

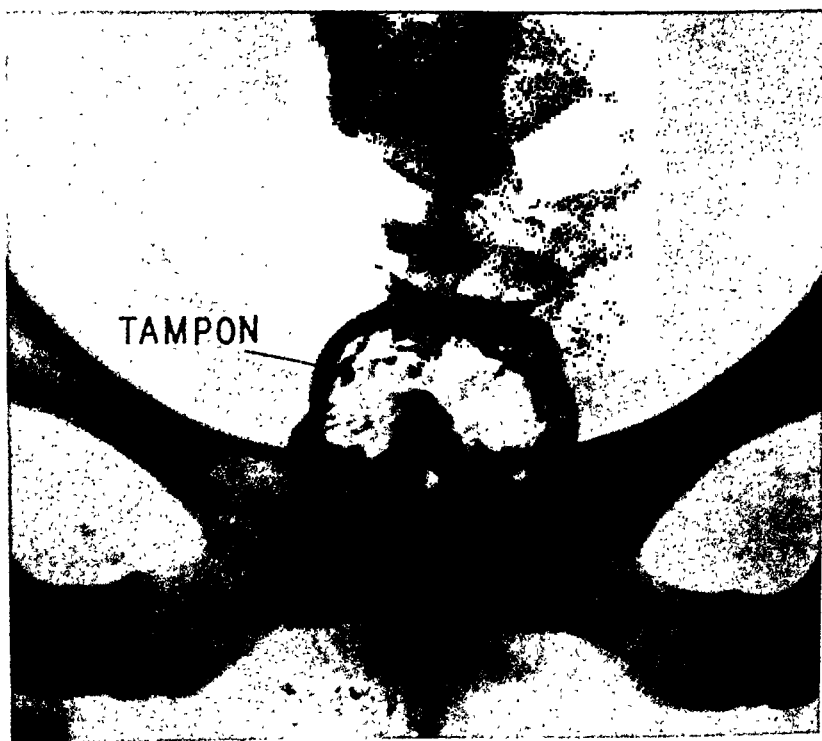


Fig. 3.—Tampon 1, showing tampon in position 20 minutes after insertion.

*Tampon dimensions given are those obtained at the time of the study.

gether by means of a waterproofed cord with double ends which hang loosely for a distance of about 5 inches, and which provide for the removal of the tampon. The surface of tampon No. 1 is soft, and pieces of cotton slough off on very slight handling. It is wrapped individually in cellophane, and according to the manufacturer's leaflet, is sterilized after being wrapped.



Fig. 4.—Tampon 2, shows tampon in vagina immediately after insertion.

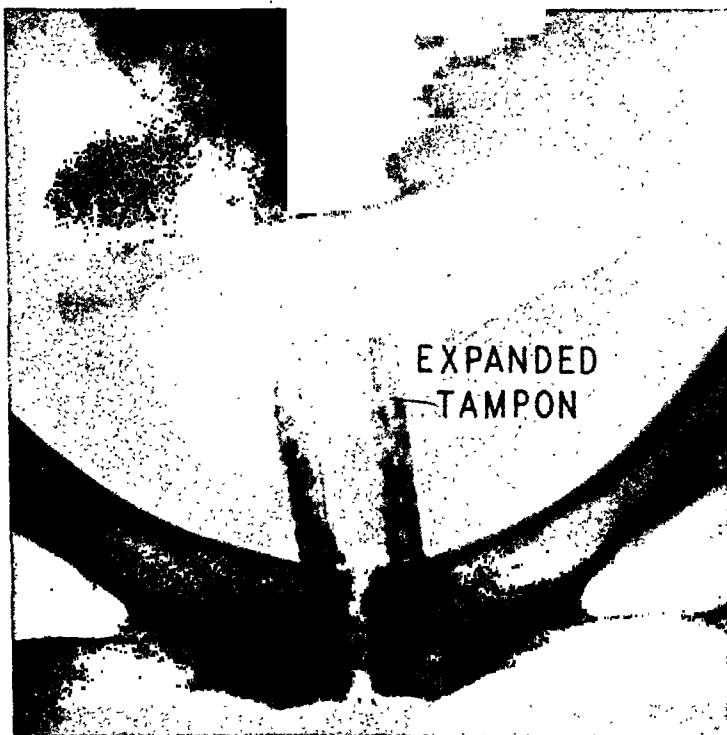


Fig. 5.—Tampon 2, shows expanded tampon 30 minutes after insertion.

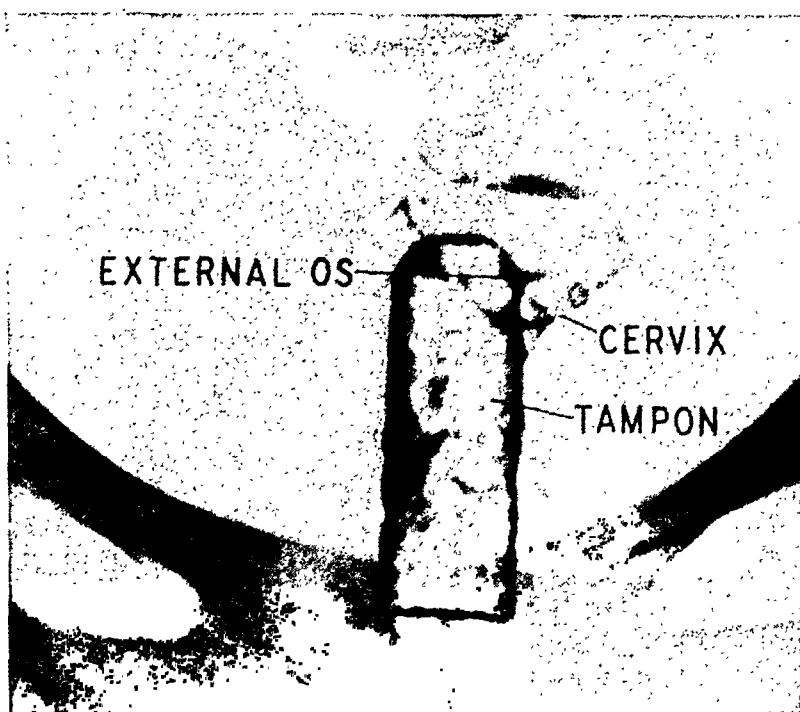


Fig. 6.—Tampon 3, shows tampon in vagina immediately after insertion.

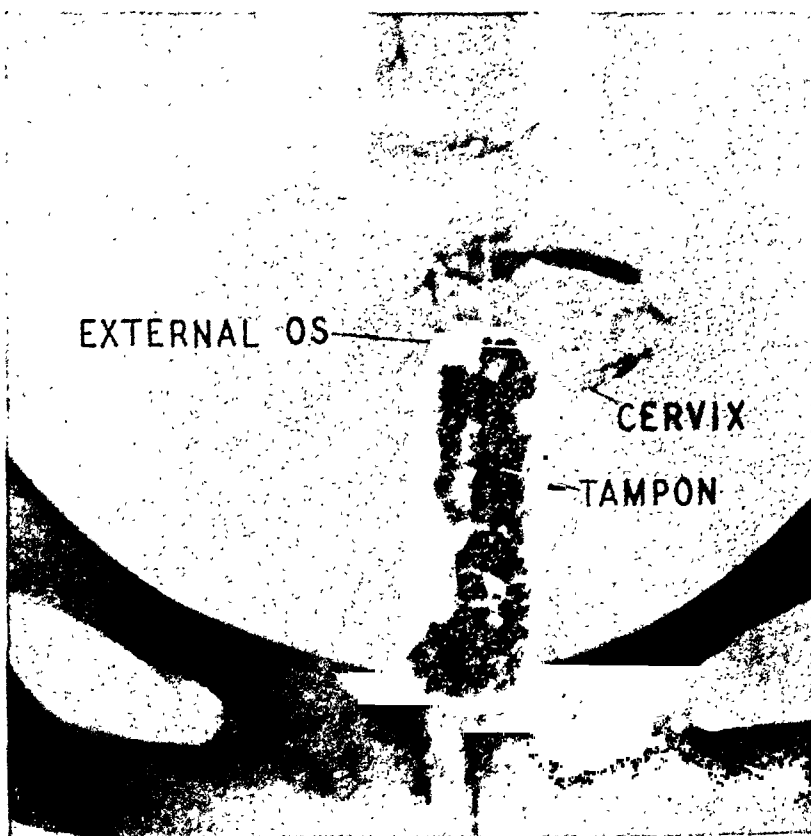


Fig. 7.—Tampon 3, shows tampon 20 minutes after insertion.

Tampon No. 2 consists of a strip of surgical cotton, approximately $2\frac{1}{8}$ inches in width and 7 inches in length, that is wound on itself with a string in its core to produce a loosely wound roll, approximately $\frac{3}{4}$ of an inch in diameter and $2\frac{1}{8}$ inches in length. Lateral compression on 6 sides results in a final diameter of $\frac{3}{8}$ of an inch with no alteration of the length by compression. The tampon ready for use measures $2\frac{1}{8}$ inches in length and $\frac{3}{8}$ of an inch in diameter. Both the pointed end and base are somewhat rounded. This tampon is wrapped in cellophane in packages of 2 and 4.

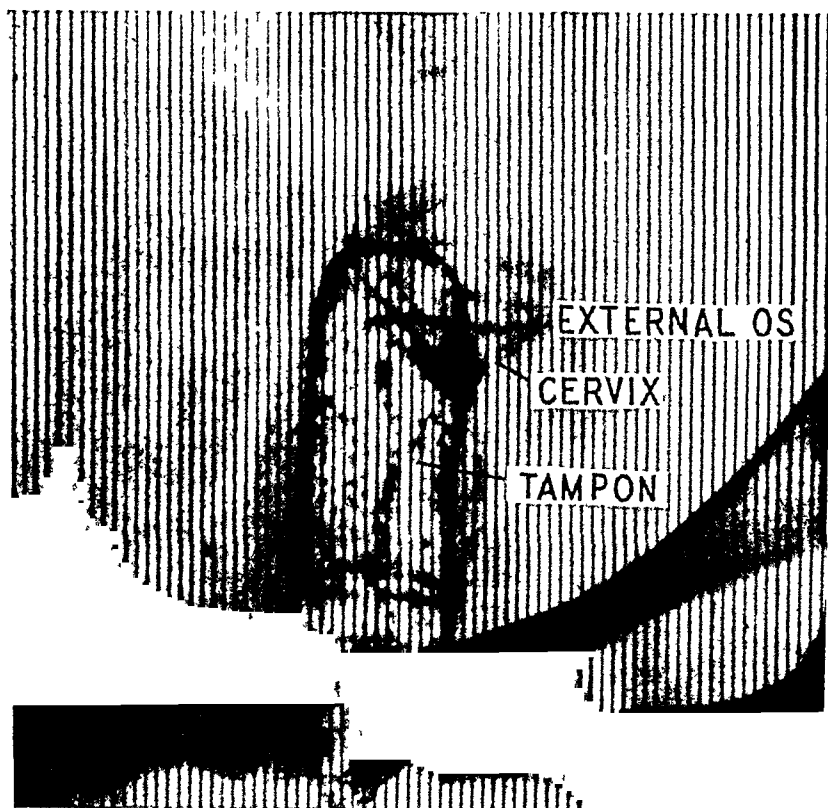


Fig. 8.—Tampon 4, shows tampon 20 minutes after insertion.

Tampon No. 3 is individually wrapped in cellophane and is nonextending. It measures approximately $2\frac{1}{8}$ inches in length and $\frac{1}{16}$ of an inch in diameter, and has a draw string anchored by means of a chain-lock stitch about $\frac{1}{4}$ of an inch from the base which permits $3\frac{1}{2}$ inches to hang free for removal. The pointed end is well beveled, covered with a sizing substance, to anchor the "quilting" threads which interlace diagonally along the sides of the base. There are two layers of "quilting" threads one on the outside overlying the thin layer of cotton which itself covers a core consisting of a roll of cellulose, bound together by the other layer of "quilting" threads. The base of this tampon is square cut.

Tampon No. 4—this is an uncompressed type of tampon that measures $2\frac{1}{4}$ inches in length and $\frac{3}{4}$ of an inch in diameter. It consists of a roll made from a strip of surgical cotton approximately $8\frac{1}{2}$ inches in length and $2\frac{3}{8}$ inches in width. The pointed end is well beveled and coated with a sizing substance to aid in the maintenance of shape and smoothness. A strip of cellophane $1\frac{3}{8}$ inches in width is wrapped around the body of the tampon and anchored about $\frac{1}{4}$ of an inch from the base edge by means of a draw string. The cellophane strip is perforated by

numerous holes $\frac{1}{16}$ of an inch in diameter. The base of this tampon is square cut and the draw string is well anchored with a chain-lock stitch placed about a half inch above the base of the tampon, allowing the ends of the string to hang free for approximately $3\frac{1}{2}$ inches.

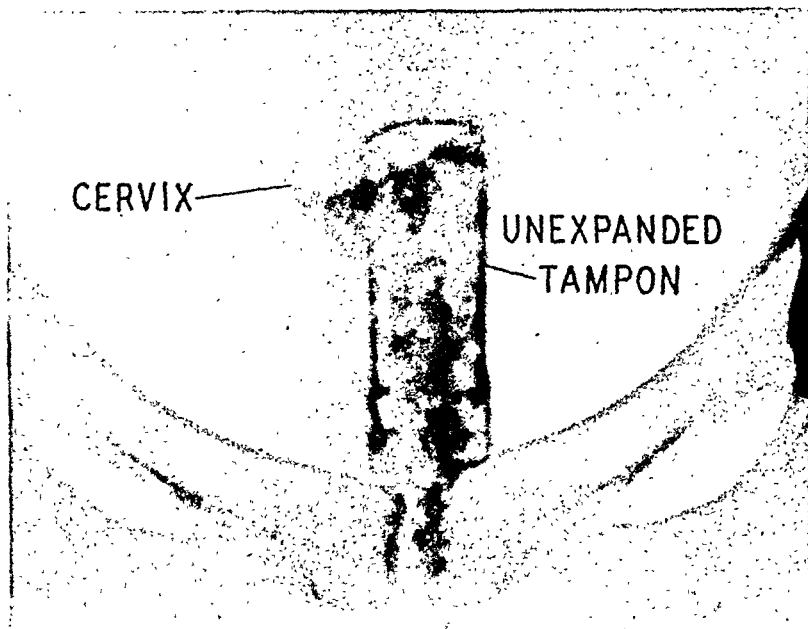


Fig. 9.—Tampon 7, shows tampon in vagina immediately after insertion.

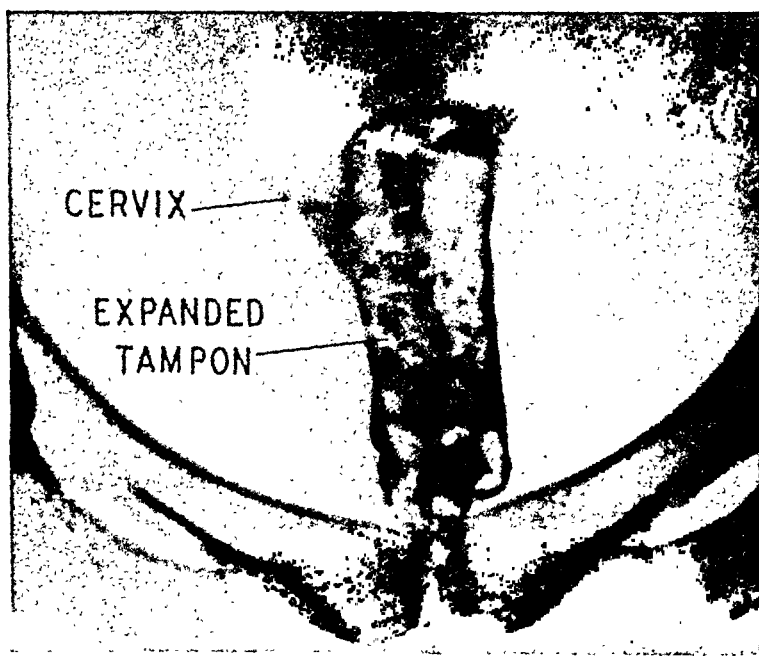


Fig. 10.—Tampon 7, shows tampon 40 minutes after insertion, showing expansion.

Tampons No. 7 and No. 12 are compressed tampons packed in mechanical inserters designed to place the tampon within the vaginal canal.

Tampon No. 7—this tampon is individually wrapped in cellophane and comes in three sizes—junior, regular and super. In this study, the regular size is considered as an average to compare with the other tampons which come in one size only.

The inserter consists of two tubes of highly glazed paper telescoping within each other. The outer tube is $2\frac{3}{4}$ inches in length and $\frac{9}{16}$ of an inch in diameter. The inner tube is 3 inches in length and $\frac{1}{2}$ of an inch in diameter. The tampon consists of a strip of surgical cotton approximately $1\frac{1}{4}$ inches in width and 4 inches in length. Through the length of the tampon, there is a cord sewn in by means of a lock stitch. Compression in two directions produces a tampon approximately $\frac{1}{2}$ inch in diameter and 2 inches in length, which is placed within the outer tube of the inserter so that a short tuft of the tampon projects from within the tube for a distance of a little over $\frac{1}{8}$ inch. This tuft by virtue of slight expansion of the cotton fibers forms a mushroom wedge over the end of the tubing. The removal string is approximately $4\frac{1}{4}$ inches in length. Insertion is effected by means of pressure on the inner tube which acts as a plunger when the outer tube is inserted in the introitus.

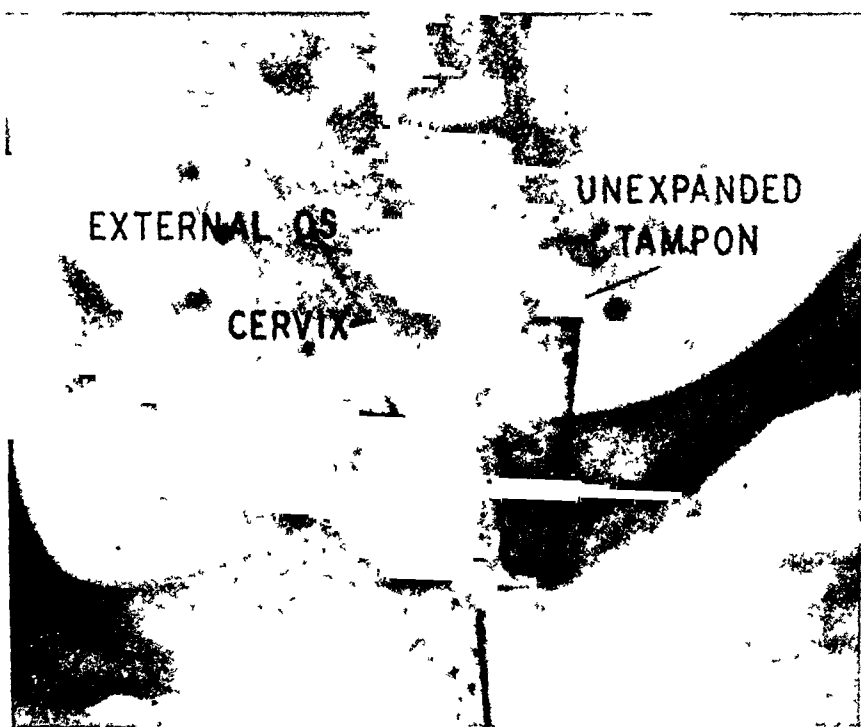


Fig. 11.—Tampon 12, shows tampon in vagina immediately after insertion.

Tampon No. 12—this is a compressed type of tampon made of a 4-inch square of cotton with two lateral edges folded to the center to form a strip 4 inches long and 2 inches wide, with fibers running lengthwise. A chain-lock loop of cord encompasses the middle of this strip before it is folded in half. A double length of cord hangs free from the tampon for a distance of about $3\frac{3}{4}$ inches. Compression and shaping results in a tampon measuring approximately $1\frac{1}{2}$ inches in length and $\frac{9}{16}$ of an inch in diameter with a hollow core extending almost the entire length of the tampon. When fully expanded, the length never exceeds 2 inches which is the length of the folded strip before compression. The inserter consists of an outer tube of kid-glazed paper approximately 3 inches in length and $\frac{5}{8}$ of an inch in diameter. The outer tube or casing has a finished edge at its open end which enters the vagina during insertion. The closed end holds the inner tube or plunger in place. The two ends of the plunger are flared outward to prevent dislocation of the two parts during use. The tampon is entirely contained within the inserter, and the strings protrude from the free end of the plunger. The entire unit is individually wrapped in transparent parchment paper.

In this study of tampon No. 1 (the nonexpanding cotton ball type), it was considered inadequate in 3 instances; adequate in 12. None reported discomfort and only one reported a clot. The insertion of this nonexpanding "cotton ball" type of tampon is difficult. Incomplete insertion within the introitus is the usual result, but the softness accounts for the lack of discomfort felt. Contamination is unavoidable.

In the use of tampon No. 2 (fixed length of $2\frac{1}{8}$ inches with lateral expansion only): Protection was considered adequate in 14 instances, with one report of leakage after 3 hours. It was reported comfortable in 8 instances, with 7 reports of slight discomfort at the introitus. There were 4 reports of a few small clots, and 11 of no clots. In the use of tampon No. 2, discomfort at the introitus in almost one-half of the cases is caused by the length of the tampon. Insertion is also a problem since contamination of the vagina cannot be avoided, and placement within the introitus cannot be readily accomplished.

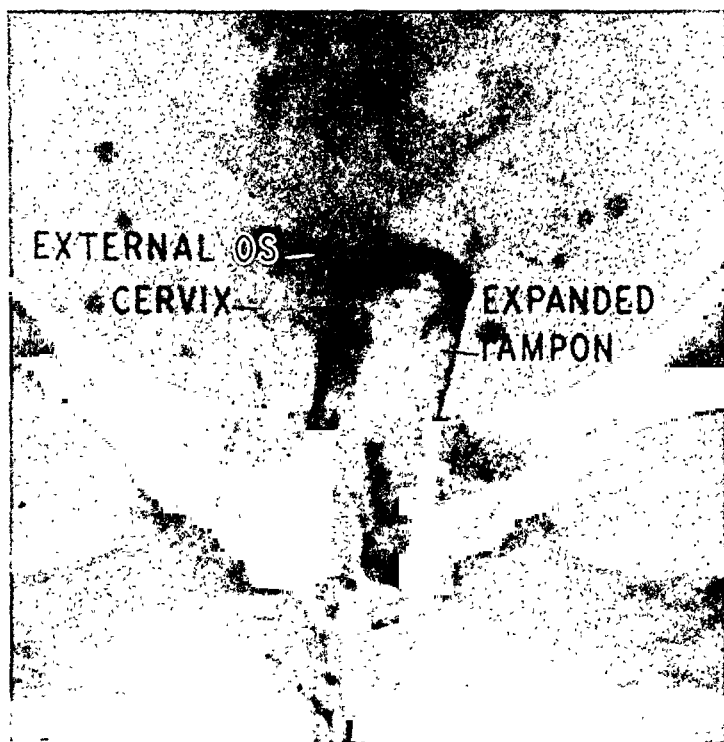


Fig. 12.—Tampon 12, shows tampon 60 minutes after insertion showing expansion.

Study of tampon No. 3 (nonexpanding). Protection was reported adequate in 12 instances, inadequate in 2. The tampon was comfortable in 5 instances, slight discomfort was reported in 6 instances. In 13 instances, there were no clots, in 2 a few small ones. In the use of tampon No. 3 discomfort at the introitus is caused by the length of the tampon. Insertion without contamination is difficult, and placement within the introitus is not readily accomplished.

Study of tampon No. 4 (nonexpanding). Protection was reported adequate in 11 instances; inadequate in 4. It was comfortable in 4 instances, but there were 4 complaints of discomfort at the introitus, 2 complaints of "burning," one of pain due to the length of the tampon, and one of a feeling of "heaviness." Discomfort at the introitus and the other complaints in the use of tampon No. 4 indicate that this tampon

TABLE I. PHYSICAL EXAMINATION OF WOMEN USED IN STUDY OF TAMPONS

| CASE | EXTERNAL GENITALIA | VAGINA (DEPTH) | CERVIX | UTERUS | ADNEXA |
|------|-----------------------|-------------------------------------|------------------------|--|---|
| 1 | Normal | 3 inches | Infantile | Infantile anterior | Slight tender- ness |
| 2 | Normal | 4 inches | Erosion Small | Small anterior | Negative |
| 3 | Normal | 4 inches Narrow | Nabothian cyst | Small anterior | Negative |
| 4 | Relaxed | 4½ inches Rectocele Cystocele | Slightly en- larged | Enlarged an- terior Fibrotic Tender | Negative |
| 5 | Relaxed | 4½ inches Rectocele Cystocele | Prolapsed | Small 3-inch retrover- sion | Thickening in left fornix |
| 6 | Normal | 3½ to 4 inches | Infantile | 3-inch retrover- sion | Mass—left fornix |
| 7 | Normal | 3½ inches | Normal | 3-inch retrover- sion | Mass—left fornix |
| 8 | Normal | 4½ inches | Soft | Slightly en- larged Tender | Thickening and tenderness in fornices |
| 9 | Normal | 4 inches | Normal | Small anterior | Negative |
| 10 | Normal | 2½ inches | Erosion Infantile | Small anterior Small fibroid | Negative |
| 11 | Normal | 3½ inches | Infantile | Infantile anter- ior | Negative |
| 12 | Normal | 4½ inches | Normal Lacerated | Small anterior | Negative |
| 13 | Normal | 3½ to 4 inches | Small | Small 3-inch retrover- sion | Negative |
| 14 | Relaxed | 4 inches | Normal Lacerated | Small 3-inch retrover- sion | Thickening in left fornix |
| 15 | Normal | 4½ inches | Normal | Small | Negative |
| 16 | Normal | 3 inches | Elongated | Small 3-inch retrover- sion Nontender | Slight thicken- ing and ten- derness in fornices |
| 17 | Normal | 3½ inches | Erosion (healing) | Small 3-inch retrover- sion | Negative |
| 18 | Normal | 3½ inches Narrow | Slight erosion | Small anterior | Negative |
| 19 | Relaxed Gaping | 4½ inches | Lacerated Erosion | Small anterior Retrocessed Small fibroid | Negative |

TABLE I—CONT'D

| CASE | EXTERNAL GENITALIA | VAGINA (DEPTH) | CERVIX | UTERUS | ADNEXA |
|--|--|-----------------------|---|---|--|
| 20 | Relaxed Gaping | 4 inches | Lacerated | Slightly en- larged Fibrotic | Right and left ovaries pro- lapsed |
| This woman has undergone operation for menorrhagia and metrorrhagia which she complained of, before being used in tampon series. | | | | | |
| 21 | Normal | 4 inches | Normal | Small anterior | Negative |
| 22 | Normal | 3½ inches | Erosion | Small | Negative |
| 23 | Gaping Relaxed Slight ir- ritation Frothy discharge | 4 inches Cystocele | Lacerated | Small anterior | Negative |
| 24 | Normal | 4 inches Rectocele | Lacerated Eroded Bleeding from external os | Small anterior | Tenderness in fornices |
| 25 | Normal | 4 inches | Small | Slightly en- larged 1-inch retrover- sion Drawn to left | Negative |

is too long for the average woman. Insertion by the fingers results in contamination, and placement within the introitus is difficult and not always completed. In 14 instances, no clot was found, one report mentioned a few small clots.

Study of tampon No. 7 (2-way expansion). Protection was reported adequate in 7 instances; 8 reported leakage. No discomfort in 9 instances, but 6 complaints of discomfort at the introitus or a "heavy" feeling. Proper placement of tampon No. 7 without contamination is aided by the use of an inserter. Placement within the introitus accounts for the lower incidents of discomfort, although the tampon is too long for the average vaginal tract. It displaces the cervix or expands outwardly to cause discomfort. No clots in 13 instances; one with a few small ones.

Study of tampon No. 12 (2-way expansion). Adequate protection reported 11 times; one report of leakage and 3 of slight leakage. Thirteen reports of "comfortable"; 2 of slight discomfort. Eleven reports of no clot; 3 of a few small clots. The use of an inserter with a shorter tampon reduces the incidents of discomfort if proper placement is accomplished. Contamination is avoided. In this and in all the previous studies, the absence of clots on the tampons in the greater number of cases is significant, since it proves that menstrual blood is not dammed back by the presence of a tampon within the vagina.

PART II

Roentgenogram visualization of the position and action of catamenial tampons within the vaginal tract was undertaken. Difficulty was encountered until a radiopaque substance could be prepared that would

mix well with menstrual blood in the vagina. It was considered desirable to develop a technique whereby the tampons could be inserted and observed.

The cervix and the vagina were well exposed by means of an O'Sullivan-O'Connor vaginal speculum, and the walls thoroughly swabbed with a preparation compounded in the following manner: Ten grams of sodium tetraiodophenolphthalein were dissolved in sterile water to make a saturated solution, to which sufficient powdered gum acacia (approximately 2 to 3 grams) was added to thicken the solution. This preparation was allowed to stand one hour before use, with frequent thorough stirrings. The use of this preparation resulted in a soft outline of the vagina and cervix. The tampons were dusted with dry powdered barium sulfate before insertion, resulting in a sharper outline. Exposures were made after preparation of the vaginal tract, and again after insertion of the tampons. In the case of compressed tampons, exposures were made again after an interval to allow expansion to take place. The tampons were inserted by the women themselves.

Summary

1. A study of 6 commercially manufactured tampons used for the control of the menstrual flow in women was conducted on a group of 25 women of varying ages and pelvic types.

2. Five of the 25 women subsequently desired childbearing and succeeded, indicating that the use of tampons does not prevent conception.

3. Nine of the 25 women had used tampons at some time previous to this study indicating a fairly widespread acquaintance with the use of tampons as a method of controlling the catamenial flow.

4. Description of the amount of flow by a patient is not always consistent with the number of pads used, indicating that adequate protection can be judged only by correlating the length of complete protection with definite amount of menstrual flow, which can be determined only by weight.

5. Seven of the 25 women had cervical erosions, but only 2 of the 7 had used tampons previously. Of the 2 who had used tampons previously, one had a lacerated cervix resulting from childbirth, and the other had an erosion which is commonly classified as a congenital erosion of the cervix.

A shorter tampon is to be preferred, since its use is least likely to cause pressure against the cervix.

6. Four of the 6 tampons were inserted manually by the women, and 2 were inserted by the use of individual inserters. The use of an inserter permits proper placement of the tampon within the vaginal tract without contamination by the fingers.

7. Three of the 6 tampons are of the nonexpanding type with a fixed length. Tampon No. 1 is the shortest being only $1\frac{3}{8}$ inches. Tampon

No. 3 and tampon No. 4 are both over 2 inches in length. Clinical findings favor the shorter tampon.

8. The remaining 3 tampons are of the expanding type. Tampon No. 2 has a fixed length of $2\frac{1}{8}$ inches, and expands only laterally. The other two expand both laterally and lengthwise. Tampon No. 7 has a fixed length of 4 inches before compression, and the other tampon No. 12, has a fixed length of 2 inches before compression.

9. Roentgenogram visualization of the position in action of catamenial tampons indicates that tampons approximately 2 inches in length are least likely to deflect the cervix, in the average woman. Tampons with a rounded base are readily removed.

The study taken as a whole leads to the conclusion that catamenial tampons can be used by the average woman to control an average catamenial flow with safety, comfort, and complete protection, provided that a short tampon is properly placed well within the introitus.

The author wishes to express her appreciation to Dr. Benjamin P. Watson, professor of Obstetrics and Gynecology, Columbia University for his interest in and supervision of this study.

VAGINITIS TREATED WITH AN ANTISEPTIC BUFFERED ACID JELLY*

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THAT leucorrhea remains as a present-day problem is borne out by Polak's statement that 85 per cent of women, married or single, have infected cervixes.¹ Many publications report figures indicating that *Trichomonas vaginalis* infections are present in 25 to 33 per cent of women.

Recently, several papers have appeared in the literature regarding the effective use of buffered acid jellies in the treatment of various vaginal infections. The change to present-day conceptions of vaginal physiology may be summarized by the editor's statement in the Yearbook of Obstetrics and Gynecology, 1943,² "During the past few years we have come to recognize the importance of the pH of the vagina. Nearly all vaginal infections can be more readily cured by maintaining a low pH medium than by any other method of treatment. Regardless of the drugs used, the important consideration is the pH."

In an extensive and excellent study of vaginal infections, Rakoff and Casper,³ utilizing an original x-ray technique, reported interesting results following the use of different products. It was concluded that water-dispersible jellies, adjusted to the proper acidity (pH 4.0) are preferable as bases for solutions, suspensions, antiseptics, fungicides, sulfonamides and estrogens. Conversely, capsules and tablets were not satisfactory. A practical point is that the medication may be continued by the patient at home.

Chrisman,⁴ using a buffered acid jelly reported excellent clinical response in 100 of 129 cases within seven weeks. These included non-specific vaginitis, cervicitis, trichomonas vaginitis, cervical erosions, and vulvar and urethral irritations. Definite relief and improvement occurred in one to two weeks. An interesting observation was that the average pH of the posterior fornix prior to therapy was 7.8 and often as high as 8.0 or 9.0. Following administration of buffered acid jelly, within six weeks, the midvaginal pH was 4.0 to 5.0 and the pH of the posterior fornix 4.5 to 5.5.

From 1936 to 1940, Roblee⁵ reported definite clinical response with the use of anhydrous lactose to create a vaginal environment of pH 4.5.

Roblee,⁶ 1943, combined a buffered acid jelly (pH 4.0 to 4.5) with a sulfonamide and obtained satisfactory results in 112 cases of conization of the cervix and 71 cases of vaginitis. He concluded that buffered acid jellies are of value in the management of cervicitis, vaginitis (especially trichomonas), and monilia infections.

*Caprokol Jelly, which consists of hexylresorcinol 1:1,000 in a buffered base titrated to a pH of 2.0, was generously supplied for this study by Dr. Earl L. Burbidge, of the Medical Research Division of Sharp & Dohme, Philadelphia, Pa.

Allen and Baum,⁷ 1942, reported 282 patients treated by means of vaginal instillations of acid buffered water-soluble jellies. The pH as well as medicaments were varied. They found that nitrazine paper was sufficiently accurate to measure pH, the results having checked within a range of 0.5 when compared with the Beckman potentiometer. The authors conclude in part, that a buffered acid jelly is an effective and acceptable method for the treatment of vaginitis, providing symptomatic relief (84 per cent of patients) and causing apparent cures in monilia and nonspecific infections.

In 1940, Bland and Rakoff,⁸ used a buffered acid jelly at pH 2.5 to 4.6 and found it extremely useful in the treatment of nonspecific infections of the vagina, cervicitis, endocervicitis, traumatic injuries and in the alteration of the vaginal flora.

Karnaky,⁹ in an extensive review study, found that the most important factor in treating trichomonas vaginitis was the pH, and that to be effective, solutions, tablets, powders or jellies should be pH 5.0 or lower.

Vaginal physiology is characterized by cyclic changes. In childhood and after the menopause, estrogenic production is at a low level, the glycogen content of the vaginal epithelial cells is decreased or absent, and Döderlein's bacilli are usually not present. These factors produce an alkaline environment in the vaginal tract which is conducive to the growth of pathogenic organisms and organisms which are not normally a part of the vaginal flora (*B. coli*, *staphylococci*, *streptococci*, *trichomonas*, *monilia*, etc.). The normal acid reaction is determined by the glycogen content of the vaginal cells, which in turn, is dependent on the estrogenic level present. Döderlein's bacilli, which are acid forming organisms, utilize the available glycogen and maintain a pH of between 4.0 to 5.0. This is an unsuitable environment for pathogenic organisms, the majority of which require an alkaline medium for growth and reproduction.

The present study was instituted with the object in mind to provide replacement therapy locally in an attempt to cause a rapid return to normal and physiologic conditions within the vagina.

In 1931, Greenhill¹⁰ reported the effective use of hexylresorcinol solution in combating *Trichomonas vaginalis* infections. Moore,¹¹ in 1941, reported the use of a water-soluble jelly containing hexylresorcinol in the treatment of trichomoniasis. The solution was found to be efficacious, but uniformly excellent results (87 per cent) were obtained in Moore's study. The jelly also used in Greenhill's study of 145 patients, is buffered and maintains a pH of 2.0. In addition, hexylresorcinol 1:1,000 provides an effective germicide with a low surface tension which is of definite value in reaching the entire surface of the vagina, and also adds local anesthetic and antipruritic activity. Other similar jellies do not provide as low a pH as the preparation used in this investigation and those referred to above.

The following types of cases were treated with this preparation:

| | |
|--|----|
| Trichomonas vaginitis | 13 |
| Monilia vaginitis | 3 |
| Pruritic vulva | 5 |
| Nonspecific vaginitis | 10 |
| Postpartum cervicitis | 14 |
| Postpartum vaginitis, without appreciable cervicitis | 12 |
| Antepartum vaginitis, of which 10 showed trichomonas | 36 |
| Postpartum vaginitis with erosion | 20 |
| Tender episiotomy scar with vaginal hyperemia | 4 |
| Senile vaginitis | 2 |
| Vaginitis in nullipara with dysmenorrhea | 1 |
| Vaginal surgery with postoperative discharge | 3 |
| Venereal warts in obstetric patients | 5 |
| Hypo-estrinism | 4 |
| Vaginitis—nonspecific treated with Caprokol Jelly and Stilbestrol | 12 |
| Acute vulvitis | 1 |

At the time of the first examination, pH determinations were made using pHydrion paper.* The container for this paper shows color indicators for a pH ranging from 1 to 11. This paper, when tested with the hexylresoreinol jelly showed a pH of approximately 1.0. Specimens for estimations of the pH were taken from both the cervix and vaginal wall with a cotton applicator, or with a bulb on a glass rod used for aspirating vaginal secretions.

Vaginal smears were made and stained in representative types of cases. The appearance of the cells and the pH of the vaginal secretions depends upon the menstrual cycle and the amount of inflammatory reaction present.

The patient is provided with specific instructions regarding the use of this preparation. She is advised either to boil the glass applicator, or to cleanse it with rubbing alcohol before inserting into the vagina. The jelly is instilled twice daily, morning and evening, during the acute stage of an infection. One application consists of approximately 5 c.c. of the preparation. Should the vaginal discharge be extensive, a perineal pad may be used. Rapid improvement occurs, within one to two weeks and the instillation of the jelly can be reduced to one application daily. A boric acid douche is advised before the patient reports for examination and follow-up study.

The earliest the jelly has been given to pregnant patients was in the second month and the latest, the eighth month. The jelly may be used without danger of introducing infection which might occur when an irrigation or douche is employed.

Patients with pelvic pathology other than cervicitis and vaginitis were excluded from this study. Hexylresoreinol jelly has been utilized in a wide variety of conditions. Numerous reports are available including various types of medication used in the treatment of vaginal infections. In postpartum cervicitis, it was found that the medicated jelly with a pH of 2.0 controlled the infection promptly and as efficiently as douches, tampons or powders. In four of fourteen patients, it was necessary to

*Manufactured by the Central Scientific Co.

coagulate the cervix. In twenty cases of postpartum vaginitis with cervical erosion at the six weeks' examination period, all but one had a complete reversal of the pathologic condition after a course of treatment with the jelly.

It has been observed that in comparison with other methods used to correct the majority of vaginal infections, the preparation used in this study has been the most effective agent yet available in healing erosions and allied infections. It must be noted, however, that a certain percentage of patients has presented recurrences of infections and during the wartime shifting of population, it has been difficult to follow most patients long enough to be certain of permanent results. Ten per cent of patients found to have acquired a *Trichomonas vaginalis* infection have shown recurrence or reinfection, and have returned for further therapy with the jelly.

Additional evidence that this jelly is a valuable addition to our armamentarium is the fact, that patients who have used various douches, powders and other agents have stated that nothing else has given as rapid relief, or is as easy to use as is the hexylresorcinol preparation.

Postpartum vaginal discharge appears to occur more frequently in nervous individuals. Our findings in these cases show a hyperemic and tender mucosa, excessive cervical secretions and usually an alkaline pH.

The results indicate that the medicated jelly employed throughout this investigation is probably most useful during the antepartum and postpartum period. As pregnancy progresses, there is a marked increase in alkaline cervical secretions. Immediately post partum for a few weeks, this is also true. It requires approximately six weeks following delivery before the vagina acquires an acid reaction and returns to the normal physiologic condition. The use of this preparation in the antepartum and postpartum periods is of definite aid in counteracting and controlling the infections which are prone to develop as the vaginal pH increases.

No cases of toxicity or reaction to the jelly were encountered.

Conclusions

1. A series of 145 patients presenting a variety of infections has been studied.

2. "Caprokol" Jelly is a definite aid in the treatment and control of these infections.

3. Normal vaginal physiology is more easily maintained and pathologic conditions reversed.

4. A buffered acid jelly with a pH in the range of 2.0 or less and possessing antiseptic, mildly analgesic and antipruritic properties offers definite advantages in the treatment and control of vaginal infections.

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TRUE KNOTS OF THE UMBILICAL CORD

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TRUE knots of the umbilical cord are not infrequent and are occasionally of a complicated nature. They are usually harmless, since they are rarely pulled tight enough in utero to obliterate completely the lumen of the vessels, or to cause the death of the fetus. They usually result from the active movement of the child. According to von Winckel, two conditions are necessary for their formation: a cord which in length exceeds twice the distance from the umbilicus to the vertex, and a small fetus or a large quantity of liquor amnii, in order to ensure mobility of the former. No doubt in many cases the knot remains open until labor begins, when the tension imparted to the cord by the descent of the fetus closes it. When the knot has been tightened during pregnancy, distortion of the cord will persist even after it has been untied, owing to the effect of the continued pressure on Wharton's jelly, while if it has formed only during delivery it can easily be straightened out. Although it is possible for the knot to become so tightly drawn as to cause a partial or complete obstruction of the cord circulation, this occurs very rarely. False knots, due to twisting or dilatation of the vessels or accumulations of Wharton's jelly, are of fairly common occurrence, and are readily distinguishable from true knots.

Baudelocque found that in some cases when two or even three knots were present, the fetus was alive and normal. Gardien stated that when the umbilical cord is very long it may become entwined around the child's neck and may even form knots which, however, can never tighten themselves during pregnancy sufficiently to cause the death of the fetus or interference with its growth. Chantreuil, on the other hand, thinks that they may be a cause of intrauterine death and that, even though born alive, the child may be thin and poorly nourished. It is commonly believed that only during labor do knots draw tightly enough to cause fetal death.

Complete absence of movements following extreme fetal activity is significant and is sufficient for a diagnosis when no other reason for this condition can be found. It is no doubt due to the gradual asphyxiation of the fetus from tightening of a knot previously formed.

Tardieu (quoted by Browne) made a knot in an umbilical cord, and after pulling it as tightly as possible pumped fluid into the cord. He found that the fluid would always pass through the knot, which partially untied itself when the vessel in front of it became swollen enough to exert pressure on the cord. He came to the conclusion that the fetus

could in every instance exert a degree of pressure sufficient to maintain the fetal circulation. The pulsations of the cord, by incessant repetition of the shock of pulsation, favor the loosening of the knots. Browne went further with the same sort of experimentation. By applying different weights and pressures to the knotted cord, he showed that under certain conditions more pressure was required to force the fluid through the knot and that this pressure was greater than the fetal heart could exert. He concluded, therefore, that in some cases a knot could interfere with and even completely obstruct cord circulation. If the knot is tightened only during labor, the death of the fetus in utero is probably to be attributed to some other cause.

During labor a true knot may result from the passing of the fetus through a loop of the umbilical cord spread out in the lower uterine segment; it may form as a result of fetal movements; or it may be a possible complication of version. The formation of a knot leads to shortening of the cord, and the knot becomes tightened by the weight or movement of the fetus. This is exaggerated if, in addition, the cord is wound around the body, neck or limbs. In most cases in which the death of the fetus is attributed to a knot in the cord, we find the cord wound once or twice around the neck or body, or under the axilla.

According to Chantreuil, the formation of knots is most likely to occur between the ninth and twelfth week when the fetus is small and the movements free owing to the relatively large amount of liquor amnii. Hyrtl believes that the time of formation of the knot may be in some degree indicated by its location: thus, if it is close to the navel it was probably formed at an early period of pregnancy. Chantreuil points out, however, that owing to the slippery surface of the cord and the slackness of the knot immediately after its formation, it might slide in either direction.

An interesting case of knotting of the cord without injury to the child is reported by Fleming. A woman, 28 years of age, was delivered at full term of a large healthy boy. The cord contained two knots, one a figure-of-eight located about one foot from the placental end, the other a single knot at about the same distance from the umbilical end. The cord was 4 feet long, and both knots were loosely tied. Fleming had observed single knots in the cord in previous cases, but never two knots in the same cord.

The separate cords of twins provide excellent opportunities for unusual twisting, interlacing, and knotting, particularly when the two fetuses are encased in one amnion without a dividing septum.

Case Reports

Seven original cases are herewith briefly described, followed by a tabulation of 32 cases from the literature, supplementing the table published by Browne.

CASE 1.—Primipara, aged 28. Pregnancy normal until 48 hours before onset of labor, when unusually strong active fetal movements were felt (as though the baby had turned completely over), followed by a complete cessation of movements. Spontaneous labor and delivery of a macerated fetus (38 weeks), weighing 6 pounds, 9 ounces, and 20 inches in length. The cord was 60 cm. in length, with a true knot tightly drawn at about the middle. The vessels proximal to the knot were completely collapsed. There was a small partial separation of the placenta, otherwise condition was normal. Wassermann test was negative.

CASE 2.—Primipara, aged 22. After a normal pregnancy, she was delivered normally of a living premature child, weighing 4 pounds, 14 ounces, and 18 inches in length. The cord was 58 cm. long and contained a true knot, not tightly drawn, about 28 cm. from the placenta.



Fig. 1.—Showing one true knot tightly drawn, delivered of a dead baby (macerated).

The cord was around the right leg and right arm. The placenta was normal and the Wassermann test negative. The baby's progress was satisfactory.

CASE 3.—Para iii, aged 37. Normal pregnancy and normal delivery after four hours of labor of a 9-pound living male child. The cord was 56 cm. in length and contained two true knots, 7.5 cm. apart; the first knot 24.5 cm. from the placenta, and the second 31.5 cm. from the placenta. The placenta was normal and the Wassermann test negative. There had been no unusual symptoms prior to labor.

CASE 4.—Primipara, aged 28. Normal pregnancy, with no unusual symptoms. Labor, lasting 13½ hours, was followed by delivery of a

living male child weighing 7 pounds, 3 ounces. The cord was 66 cm. long and had two true knots; the first 30.5 cm. from the placenta, the second 41 cm. from the placenta. The placenta was normal, the Wassermann test negative. (Fig. 2.)

CASE 5.—Primipara, aged 36. Normal pregnancy, followed by normal delivery, lasting 5 hours, of a living male child. The cord was 59 cm. in length, with one true knot, 32 cm. from the umbilicus. The placenta was normal, the Wassermann test negative.



Fig. 2.—Showing two true knots, delivered of a living baby.

CASE 6.—Para ii, aged 23. Normal pregnancy; no symptoms. Normal delivery of a living female child, weighing 7 pounds, 12½ ounces, and 19 inches in length. Labor lasted 2½ hours. The cord was 61 cm. in length, with one true knot, 15 cm. from the placenta. The placenta was normal, the Wassermann test negative.

CASE 7.—Para ii, aged 38. Pregnancy was normal, but the patient noticed a cessation of fetal movements 80 hours before the onset of labor. No unusual activity had preceded the cessation. After labor lasting 1 hour and 10 minutes, normal delivery of a male macerated fetus weighing 7 pounds, 9 ounces, 20 inches in length. The cord was 74 cm. in length and contained one true knot, tightly drawn, 49.5 cm. from the umbilicus. The placenta was normal, the Wassermann test negative. (Fig. 1.)

TABLE I

| OBSERVER AND DATE | AGE | PARA | ALLEGED CAUSE | SYMPTOMS | LENGTH OF CORD | NO. OF KNOTS | SITUATION OF KNOT | VARIETY OF KNOT | PRESENTATION | REMARKS |
|-------------------------------|-----|------|------------------------|---|-------------------------------|--------------|---|--------------------------------------|--------------|--|
| Fleming 1924 | 28 | 7 | --- | --- | 48 in. | 2 | First, 1 ft. from placental end; second, 1 ft. from umbilical end | First figure of eight; second single | --- | --- |
| Atwood 1932 | 34 | 3 | --- | Pain 10 days prior to admission; unusual fetal activity | --- | 1 | Middle of cord | Sailor | --- | --- |
| Atwood 1932 | 42 | -- | --- | --- | --- | -- | --- | Cords intricately knotted | Breech | Mono-amniotic twins (male) |
| Cejeys 1936 | 23 | 1 | --- | --- | --- | -- | Close to umbilicus | --- | --- | --- |
| Cejeys 1936 | 32 | 1 | --- | --- | --- | -- | --- | --- | --- | Mono-amniotic twin 6 months; cords knotted together |
| D'Elia 1938 | -- | 1 | --- | --- | 90 cm. | 1 | 25 cm. from placenta | Double | Vertex | Forceps; asphyxiated; died shortly after birth |
| Emmanuel 1930 | 43 | 4 | --- | --- | First 80.5 cm.; second 94 cm. | 1 | --- | True | H.H.L. | Second twin died 1 hour before birth; knot drawn tight |
| Floyd 1934 | 26 | 2 | --- | --- | --- | 1 | Near junction of middle and placental thirds | True | Vertex | Heart sounds and movements normal; baby alive and well; knot not tight |
| Gallucci and Delascio 1941 | 30 | 2 | --- | --- | --- | 1 | Middle portion of cord | --- | Vertex | Cesarean section |
| Itzkin 1929 | 27 | 1 | Unusual length of cord | Fetal movements ceased 10 days before labor; no F.H. sounds | 75 cm. | 1 | About middle of cord; 36 cm. from umbilicus | Single true knot | --- | Male macerated fetus |

| Kittler 1928 | 27 | 2 | Fall; next day ab- dominal pain | Cessation of fetal movements | 45 cm. | 1 | Looped around the fetus and tied | Double true knot | Vertex | Premature macerated fe- tus |
|-------------------------------|----|----|---|---|---------|---------------|---|--------------------------------|------------------------|---|
| Litt and Strauss 1935 | 30 | 3 | ----- | Cessation of fetal movements 4 days before labor | ----- | Multi- ple | 30 cm. from placenta, entangled and knot- ted in multiple true knots | True, mul- tiple | 1. Breech 2. Vertex | Mono-amniotic twin pregnancy. (1) Anen- cephalic monster; (2) macerated fetus |
| Lundgren and Boice 1939 | 26 | 1 | ----- | Cessation of fetal movements 2 days before ad- mission | 120 cm. | 2 | ----- | Half-hitch 1 foot apart | Vertex | Macerated; dead about 4 days |
| Lundgren and Boice 1939 | -- | -- | ----- | ----- | Normal | 1 | ----- | True tied knot | Vertex | Stillborn |
| Lundgren and Boice 1939 | 30 | 6 | ----- | Cessation of fetal heart sounds be- fore delivery | 65 cm. | 2 | ----- | True | ----- | One knot very tight and proximal vessels col- lapsed |
| McCormick 1929 | 31 | 1 | Fall at 7½ months, gestation | ----- | ----- | 1 | ----- | Loose fig- ure-of- eight | ----- | ----- |
| McNally 1938 | 29 | 4 | ----- | Cessation of fetal movements 72 hours before la- bor | 62 cm. | 1 | 17 cm. from child | True | Vertex | Normal delivery; dead male child macerated |
| Mitchell 1939 | 29 | 4 | ----- | Unusually active fetal movements; ceased next day | 82 cm. | 1 | 54 cm. from placenta | True, tightly drawn | ----- | Spontaneous delivery of dead macerated child |
| Montanari 1939 | 24 | 2 | ----- | 10 days before de- livery violent fe- tal movements, lasting 1 hour, then cessation | 50 cm. | Mult. | Middle of cord | True | ----- | Believes knots are formed at early period when fetus is most ac- tive toward end of sixth month |
| Nizza 1933 | 29 | 2 | Length of cord | ----- | 70 cm. | Mult. | 50 cm. from placenta | True | Cephalic | Delivery at 7 months, twins, both living |
| Quigley 1935 | 34 | 1 | Mono-am- niotic twin preg- nancy | Only one fetal heart heard | ----- | Sever- al | ----- | True | Vertex | Stillbirths; twin cords inserted marginally 9 cm. apart |

TABLE I—Cont'd

| OBSERVER AND DATE | AGE | PARA | ALLEGED CAUSE | SYMPTOMS | LENGTH OF CORD | NO. OF KNOTS | SITUATION OF KNOT | VARIETY OF KNOT | PRESENTATION | REMARKS |
|-------------------|-----|------|---------------|--|----------------|--------------|---|-----------------|--------------|---|
| Trettenero 1928 | 27 | 2 | ----- | ----- | 101 cm. | 1 | 84 cm. from placenta | True | Vertex | ----- |
| VerHoef 1929 | 27 | 1 | ----- | No fetal movements since first pains | 70 cm. | 1 | 20 cm. from placenta | True | ----- | Stillbirth; knot tightly drawn |
| Beard T.C. 1944 | -- | 3 | ----- | ----- | 24 in. | 1 | Not given | True | Vertex | 34 weeks. Normal delivery; alive. Spina bifida. Lived 7 days; infection |
| Coulson 1944 | 26 | 1 | ----- | Fetal distress; much meconium | ----- | 1 | Not given | Glove tight | Vertex | Twice around neck; shocked. Baby made good recovery |
| Hennessy | 28 | 1 | ----- | Cessation of fetal movements 48 hours before labor | 60 cm. | 1 | 29 cm. from placenta | True | Vertex | Tightly drawn knot. Fetus macerated, 38 weeks |
| Hennessy | 37 | 3 | ----- | ----- | 56 cm. | 2 | First knot 24.5 cm. from placenta; second knot 31.5 cm. from placenta | True | Vertex | Normal delivery of a 9-pound living male |
| Hennessy | 22 | 1 | ----- | ----- | 56 cm. | 1 | 25 cm. from placenta | True | Vertex | Knot loose around right leg and right arm. Living baby (32 weeks) |
| Hennessy | 28 | 1 | ----- | ----- | 66 cm. | 2 | First knot 30.5 cm. from placenta; second knot 41 cm. from placenta | True | Vertex | Normal delivery of a living female |
| Hennessy | 36 | 1 | ----- | ----- | 59 cm. | 1 | 32 cm. from placenta | True | Vertex | Normal delivery of a living child. |
| Hennessy | 23 | 2 | ----- | ----- | 61 cm. | 1 | 15 cm. from placenta | True | Vertex | Normal delivery of a living child |
| Hennessy | 38 | 2 | ----- | Cessation of fetal movements 80 hours before labor | 74 cm. | 1 | 49.5 cm. from umbilicus of fetus | True tight | Vertex | Normal delivery of a macerated male, 7 pounds, 9 ounces, 20 inches |

Summary

1. True knots of the umbilical cord are fairly common.
2. They may exist during intrauterine life without endangering the life of the fetus.
3. They sometimes obstruct cord circulation sufficiently to cause death of the fetus.
4. Usually they are of little clinical importance.

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116 EAST 68TH STREET.

CLINICAL SIGNIFICANCE OF STRUMA OVARII

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THERE have been eight cases of struma ovarii recorded in the pathologic files of the Sloane Hospital for Women in the past 20 years. This represents 2.7 per cent of 297 ovarian teratomata of all types which were examined during the same period. In addition to these, several thyroid rests have been observed; the diagnosis of ovarian struma, however, has been confined to those tumors which contain significant quantities of thyroid tissue.

Of the eight cases reported here, seven presented the usual array of clinical symptoms and signs which ordinarily accompany benign ovarian tumors: intermittent abdominal pain, painless pelvic or abdominal masses, and, in one instance, acute abdominal pain due to torsion of the pedicle. In these cases, the presence of thyroid tissue is of pathologic interest only. The cystic tumors were generally multilocular, and three of the seven contained epidermoid elements characteristic of the ordinary dermoid cyst. Microscopically, none of these cases showed evidence of hyperplastic changes in the thyroid tissue. The eighth case, however, presented a symptom complex of an unusual nature, the diagnostic and therapeutic implications of which are deemed significant. This case is therefore presented in detail.

Case Report

Mrs. J. J., aged 53, para viii, gravida viii, presented herself at the Presbyterian Hospital in September, 1943, with the chief complaint of goiter of 35 years' duration. She was admitted to the surgical wards for study shortly thereafter, and in October, readmitted for thyroidectomy.

History: On admission, there were three groups of significant symptoms:

(a) A history of goiter-like swelling in the neck for 35 years. This had been noted after her first pregnancy, and had enlarged thereafter with each pregnancy, and also to a notable degree for the five years prior to admission.

(b) The patient had noted mild exertional dyspnea for approximately two years, and some difficulty in swallowing for several months prior to admission. She had had a relatively uneventful menopause 14 months before entry to the hospital, but since that time had experienced mild palpitation, insomnia, increased perspiration and some nervousness. Mild tremor of the fingers and increasing fatigability had been noted recently.

(c) A progressively enlarging abdominal swelling had been present for 1½ years.

Physical Examination confirmed the presence of thyroid and abdominal masses. The thyroid was enlarged to "football" size. It felt irregularly cystic and lobular. The abdominal mass was irregular, cystic and moderately mobile; it filled the lower abdomen and rose almost to the costal margin on the left. There were no eye signs of thyrotoxicosis. There was a slight tremor, and mild cardiac hyperactivity. Moderate tachycardia was constant. The blood pressure on admission was 150/70.

Laboratory Data: Basal metabolic rates were obtained ranging from +30 per cent on 9/21/43 to +61 per cent on 10/21/43. These were followed by readings of +56 per cent on 11/1/43 and +55 per cent on 11/8/43. Blood cholesterol was 161 mg./% on 10/21/43 and blood iodine 15.1 gamma/% on 10/22/43. This latter observation was made three weeks after cessation of a previous course of iodine therapy and is considered significant.

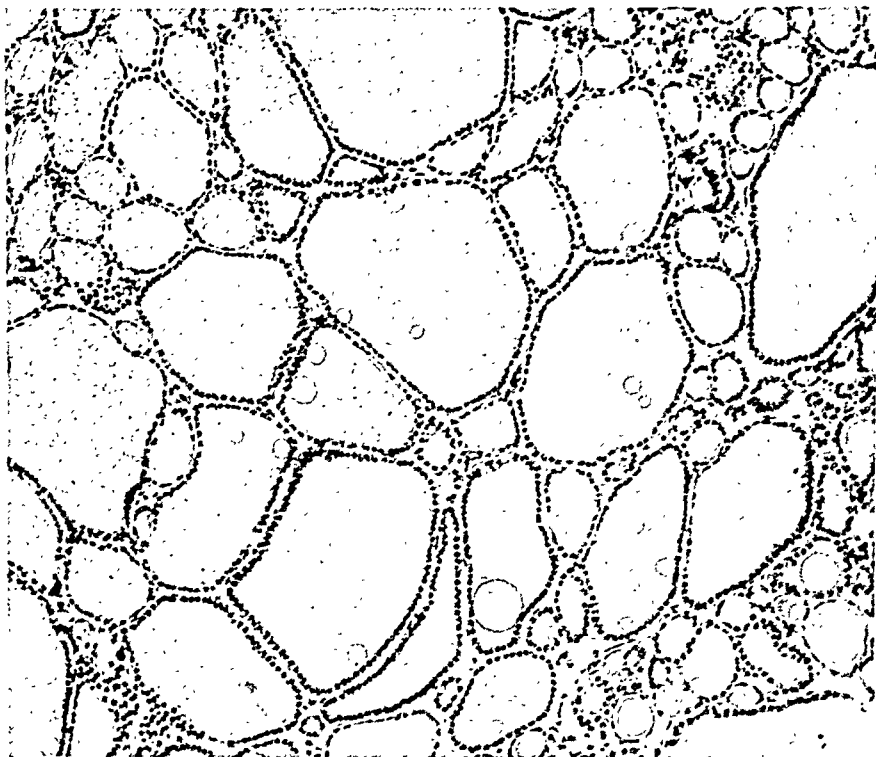


Fig. 1.—The goiter $\times 150$.

Course: On her first admission, the patient was given a course of iodine therapy which consisted of 1 c.c. of Lugol's solution daily for 12 days. This had no perceptible effect on her general status. On readmission, another course of Lugol's solution had a slight ameliorating effect on her pulse and symptoms, but none on the basal metabolic rate.

Since the abdominal tumor was regarded as an ovarian cyst, it was deemed advisable to deal with the thyroid problem first. Therefore, on 11/10/43 a partial thyroidectomy was performed. At operation, the thyroid was represented by a huge irregularly cystic nodular mass which measured approximately 26 cm. in its greatest diameter and weighed 920 Gm. on removal. Microscopic examination revealed acini which varied markedly in size; many were distended by colloid and lined by flattened cuboidal cells; a few smaller acini were lined by higher cuboidal cells. In some of the more solid portions of the gland, focal

collections of lymphocytes were seen. There were occasional areas of degeneration and old hemorrhage throughout. It was the opinion of Dr. V. Kneeland Frantz of the Department of Surgical Pathology of the Presbyterian Hospital, who examined these sections, that the bulk of the tissue was involuted; furthermore, she was not able to correlate the histologic picture with the clinical evidence of toxicity.

The patient made a relatively uneventful recovery from the thyroidectomy. A moderate to mild tachycardia persisted, but its significance was difficult to evaluate because of some anemia. The patient was improved subjectively. Her basal metabolic rate on 11/22/43 was +10 per cent. Throughout her hospital stay, she was kept on iodine therapy.

The patient was discharged home for interval convalescence; she felt fairly well in the interim and was admitted to the Sloane Hospital in January, 1944, for removal of her abdominal tumor. Upon admission, there was mild tachycardia and nervousness; the blood pressure was 170/102. No other significant symptoms or signs of thyrotoxicosis were elicited.



Fig. 2.—The struma ovarii $\times 150$.

At laparotomy on 1/11/44, a large tumor was found arising from the left adnexal region and filling most of the abdominal cavity. The uterus appeared normal; the bowel was adherent to the tumor mass in several areas but the peritoneum was otherwise clear. A supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed.

Pathologic examination revealed the endometrium to be mildly hyperplastic, and the right ovary to be the site of a small serous cystadenoma. The left ovary had been replaced by a huge multilocular tumor mass measuring 23 by 12.5 by 8.5 cm. Approximately three liters of fluid had already been removed from one locule at operation. Some locules were lined by a smooth grayish-tan membrane and contained clear yellow

fluid. About one-third of the total volume of the tumor was occupied by a honeycombed gland-like tissue which resembled thyroid tissue grossly. On microscopic examination, a variable pattern was encountered. Stratified squamous epithelium lined some of the spaces, while numerous locules were lined by a single layer of low columnar epithelium. The thyroid portions of this cystic teratoma also varied. There were some small acini closely arranged with cuboidal epithelium lining them. There were also some larger acini with low papillary infolding and low columnar epithelium. It was the impression of Dr. Frantz that the ovarian struma showed more evidence of hyperplasia and less of involution than the goiter. The possibility that the thyrotoxicosis in this case was directly related to the ovarian struma was suggested. The probability that the struma played some role in this endocrine over-activity seems inescapable.

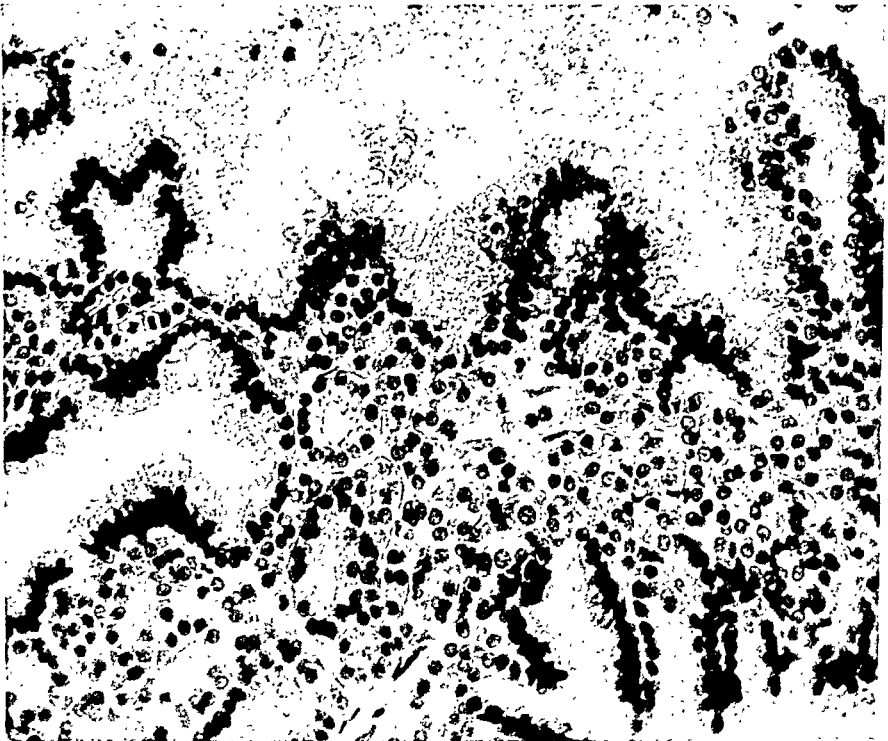


Fig. 3.—The struma ovarii $\times 300$.

The patient made an uneventful recovery from the operation, and has been well and without observed tachycardia or thyrotoxic symptoms since. The basal metabolic rate was noted at -14 per cent on 1/29/44 before discharge from the hospital, and $+1$ per cent on 2/21/44.

Discussion

The case which we have presented is notable in that a huge struma colli, a large struma ovarii, and evident thyrotoxicosis were coexistent. It is unfortunate that the possibility of ovarian struma was not considered and the preliminary work-up carried out with this in mind. Despite the incomplete data, several points of interest have been derived from the case and from the review of the literature which it has occasioned. The actual role of the ovarian tumor in the production of the

hyperthyroidism is problematical, and no amount of study of the data can produce any conclusive evidence. However, the comparative microscopic findings, the probable mechanical contribution of the huge goiter to the elevated basal metabolic rate, and the persistent tachycardia following thyroidectomy might all be considered as presumptive evidence that the ovarian tumor contributed to the thyrotoxicosis.

That struma ovarii is capable of producing or at least contributing to thyrotoxicosis, is established. It is this ability which distinguishes the ovarian struma among all ovarian neoplasms, and removes it from the category of the simple pathologic curiosity. It should be emphasized that cases of functioning ovarian struma may easily escape diagnosis, either through failure to appreciate mild hyperthyroid symptoms, or through chance avoidance of thyroid tissue in the sectioning of large ovarian teratomata. In 1940, Emge estimated the recorded cases of struma ovarii at 150, of which 5 to 6 per cent were said to have produced thyrotoxicosis.¹ Since this time, some 31 ovarian strumata have been reported;²⁻⁹ of these, eight are said to have been accompanied by thyrotoxicosis. In at least five cases, coincident enlargement of the thyroid was present. In three patients thyrotoxic symptoms were relieved by oophorectomy alone; in two of these, prior subtotal thyroidectomy had failed to arrest the hyperthyroidism.

It is of interest that in most of the cases in which such data are available, the ovarian sections have failed to show the presumed microscopic stigmata of hyperthyroidism, despite amelioration of symptoms by removal of the tumor. It would appear reasonable to consider the ovarian struma as a functioning part of the total thyroid tissue of the body, which may react to iodine lack, to the thyrotropic hormone, or to other stimuli in a manner similar to that of the thyroid gland itself. If this hypothesis is tenable, one might then consider the removal of an ovarian struma as tantamount to subtotal ablation of the thyroid gland. The signal importance of this disease picture is manifested in the case which presents distinct evidence of thyrotoxicosis, plus enlargement of the thyroid gland, plus an ovarian tumor. If the thyroid does not by its very size demand removal, as it did in the case herewith presented, the possibility of a functioning ovarian struma should be considered, and the primary surgical consideration weighed. Two cases of apparently needless thyroidectomy in such a situation are recorded in the recent literature.

Summary

The incidence of struma ovarii among 297 ovarian teratomata of all types removed at the Sloane Hospital for Women during the past 20 years is 2.7 per cent. A case is presented in which thyrotoxicosis, a large struma ovarii, and a huge goiter were coexistent. The recent literature upon struma ovarii is briefly reviewed. The clinical and therapeutic implications of this condition are considered.

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OVARIAN PREGNANCY*

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OVARIAN pregnancy is the rarest type of extrauterine pregnancy. More than 200 cases of ovarian pregnancy have been reported in the literature and all stages of development from the youngest to that of a mature fetus lodged in the ovary, have been found. The number of cases would probably be higher if a complete histologic examination were performed in all cases of hematomas of the ovary, or in those cases where rupture of a follicle or corpus luteum takes place.

According to Spiegelberg the following four requirements were postulated before the diagnosis of a true ovarian pregnancy could be made:

1. The tube on the affected side must be intact.
2. The fetal sac must occupy the position of the ovary.
3. It must be connected with the uterus by the uteroovarian ligament, and
4. Definite ovarian tissue must be found in the sac wall.

It has therefore been claimed that the majority of the cases reported were not true ovarian pregnancies, since all the necessary criteria were not present, and that only about 50 cases could be so classified.

It would seem that some of these requirements are much too rigid, since their presence or absence will depend upon many conditions. If the operation is done some time after the sac wall has ruptured, and the embryo has escaped from the sac, definite changes do take place in the involutional process that may destroy some of the evidence, or the anatomic relations may be distorted by the fetal sac itself; or by the amount of blood in the ovary itself, or clotted blood surrounding the area.

Two etiologically different types of nidation have to be differentiated in the presence of ovarian gravidity—namely, fertilization within the Graafian follicle before the ovum has escaped, or fertilization outside of the ovary. There seems to be no reason why fertilization may not take place in the tube and travel back to become implanted in a recently ruptured ovary, or it may take place outside of the tube or ovary with implantation taking place in the ovary, usually at a point remote from the corpus luteum. In the intrafollicular type, there is a failure in the mechanism of the ovum resulting in fecundation within the follicle.

Of great speculative interest in these cases, as in all types of ectopic pregnancies, is the causal relationship of the presence of endometrial nests in the organs involved. Endometriosis in the ovary is not an uncommon condition, and whether the presence of endometrium is necessary for implantation to take place is unknown. Logically, it would seem that the presence of endometrium is essential, and that implantation cannot take place in its absence.

*Presented at a meeting of The Bronx Gynecological and Obstetrical Society, May 22, 1944.

It is difficult to make a diagnosis of ovarian pregnancy. The symptoms closely resemble those of tubal pregnancy. Rupture may occur later than in the tube, there may be less uterine bleeding, the pelvic pain may not be so acute since there are little if any muscle cramps, and the tumor mass felt on examination may be longer than that of a tubal pregnancy in a corresponding period of pregnancy.

The case to be reported is, we believe, a very good example of the intrafollicular type. The rarity of the condition and the excellence of the specimen justify the presentation of the case as one of ovarian pregnancy.



Fig. 1.—(26069.) Microscopic section showing ovarian cyst wall with the presence of adjacent blood clot and chorionic villi. ($\times 300$.)

Case Report

HOSPITAL No. 152593.—Mrs. H. N., aged 30, was first seen by the senior author and the following history was obtained. White woman, married, the background of her medical and surgical history was essentially negative. She began to menstruate at the age of 11, regular 28-day intervals, lasting 5 to 6 days. Moderate flow with no pain. She was delivered spontaneously of a living child 6½ years previously.

Her last period was due December 16, which she missed. She began to bleed moderately on December 26, spotting for 6 days. She stopped

for several days and the bleeding returned. With the return of the flow, she began to have lower abdominal pain more or less constant in character and more pronounced on the left side, with frequent urination.

General examination at this time was not relevant. Pelvic examination showed the following: Moderate bloody discharge. The perineum was relaxed, the cervix bilaterally lacerated and pointing in the axis of the vagina. On attempt at motion she complained of pain in the abdomen. The fundus uteri was anterior, slightly enlarged and partially fixed. To the left of the uterus a rounded tumor mass could be palpated easily, about the size of an egg. This was fixed and quite tender. The right adnexa were normal. A diagnosis of left unruptured ectopic pregnancy was made and she was referred to The Bronx Hospital.

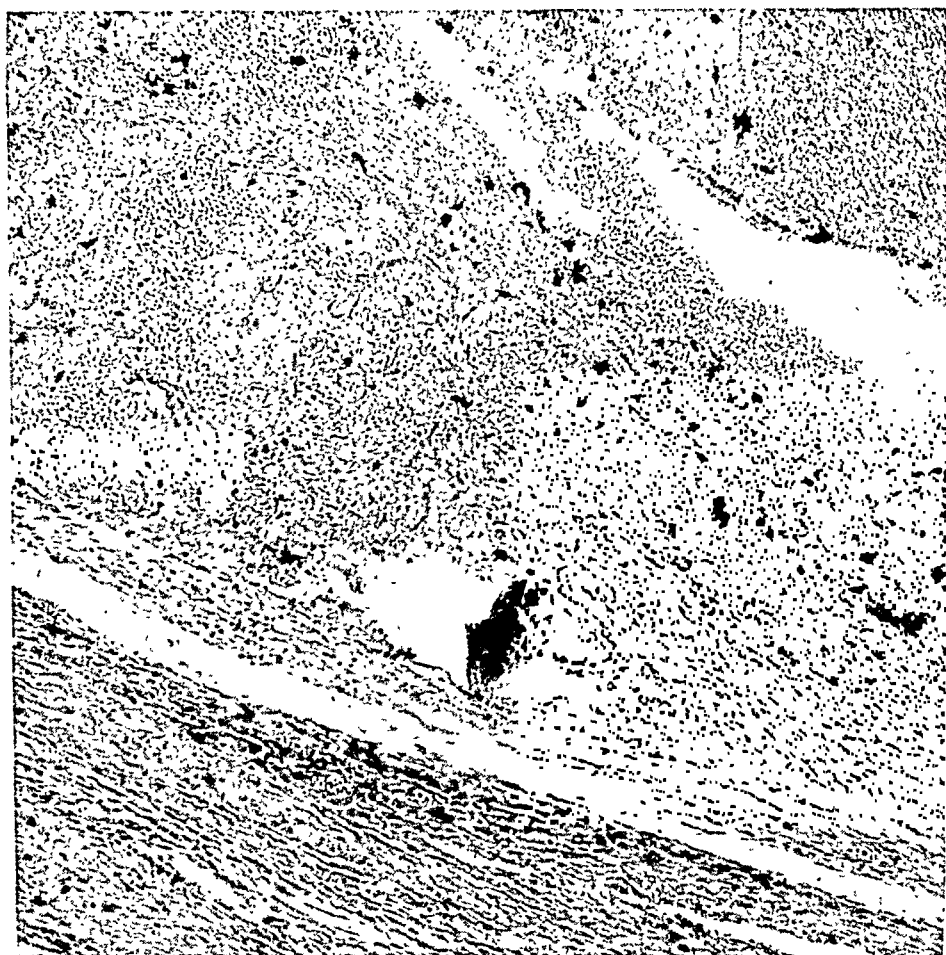


Fig. 2.—(26069.) Microscopic section showing ovarian cyst wall with the adjacent hemorrhage. ($\times 300$.)

She was admitted to the hospital on January 10, 1944, and physical examination was as described above. Pulse rate was 72, temperature 99° F., and blood pressure 130/80. The laboratory findings showed a leucocytosis of 11,000 with 61 per cent polymorphonuclear leucocytes, hemoglobin 85 per cent with red cell count of 4,370,000. Urine was negative.

Operation the next day showed the following: In the abdominal cavity, some free blood clots were found in the pelvis and covering the intestines. The left ovary was enlarged to about four times its normal

size. About one-third of the surface of the ovary (anterior) consisted of a craterlike mass filled with organized blood clots. A sharp ridge surrounded this hemorrhagic area. The Fallopian tube was normal in appearance and partly adherent to the ovary. The fundus uteri and right adnexa were found to be normal. A left salpingo-oophorectomy was performed and the abdomen closed. She made an uneventful recovery and was discharged on the twelfth postoperative day.

Pathological Report (No. 26069).—The specimen consists of a tube and ovary. The ovary measures 5 by 4 cm., and is the seat of a 3 cm. in diameter hemorrhagic area filled with friable, villous-like tissue. Its attached tube measures 5 cm., and shows no gross pathology.

Microscopically, sections of the ovary show the presence of blood and chorionic villi adjacent to ovarian stroma (Figs. 1 and 2). Sections of the tube revealed a thickened wall containing dilated blood vessels.

Diagnosis: Ovarian Pregnancy.

We are indebted to Dr. Joseph Felsen, Director of Laboratories, The Bronx Hospital, for the photomicrographs.

900 GRAND CONCOURSE

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VAGITUS UTERINUS WITH PROLAPSE OF THE UMBILICAL CORD

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IN OBSTETRIC practice, few incidents are more incredulous than vagitus uterinus, which by definition, is crying in utero. According to Freed,¹ vagitus uterinus was first described by J. B. von Fischer in 1730. However, this rare occurrence apparently was known of before this time for DeLee² wrote that Mohammed and St. Bartholomew made themselves heard while in the uterus, but he added that these were probably fables.

Kitzmiller and Mitchell³ cited three conditions which must be present in order for crying in utero to become evident, namely: (1) the membranes must have ruptured; (2) there is usually some operative manipulation to stimulate the infant; (3) there must be entrance of air into the uterus. They added that points (1) and (3) are generally accepted, but that the second point is in question, that is, whether this stimulation to the infant is central asphyxia, or merely a cutaneous stimulation.

In practically all reported cases, this phenomenon follows some manipulation as application of forceps, version or simple vaginal exploration. Freed observed vagitus uterinus following introduction of his hand into the vagina, as did Morton.⁴ In the latter's case, a version was done but the child died. In Flatau's classical case, reviewed by Freed, crying was heard as often as the prolapsed umbilical cord was compressed by the fingers. The explanation offered was that pressure on the umbilical cord would increase the carbon dioxide content of fetal blood and stimulate respiration.

It has been suggested that vagitus uterinus is a sign of fetal distress. Frazier⁵ said that his case afforded an exception to this generalization in that the mother, in gestation 31 weeks, was admitted for antepartum hemorrhage. The baby cried for forty minutes, and was delivered precipitately thirty hours later, dying of prematurity and intracranial damage, the latter being due to precipitation.

Clouston⁶ noted vagitus uterinus in a patient with brow presentation which he converted into a mento-anterior face presentation and successfully delivered.

In a mother 38 weeks pregnant, with a pelvis suggestive of disproportion, Field⁷ ruptured the membranes with a catheter and air was heard being sucked into the uterus through the lumen of the catheter; the infant cried. Fifty-four hours later, the mother delivered a normal child which lived. With delivery of the placenta, a gush of air came from the vagina.

Several cases of vagitus uterinus have been reported in connection with "high forceps." Brodhead⁸ had one case and Pease⁹ three. High forceps delivery was attempted unsuccessfully in a case recorded by Harrison,¹⁰ and the patient was subsequently delivered of a living 10-pound infant by cesarean section.

Babies who cry in utero have been delivered alive several days after the occurrence. Rucker¹¹ reported two cases and concluded that the fetal mortality in cases of vagitus uterinus, while not excessive, seems to be due largely to efforts to save the baby from asphyxia by rapid delivery.

If a baby cries in utero, will it drown? Peters¹² said that theoretically, intrauterine crying would entail the danger of the baby drowning in the amniotic fluid, but in practice, this apparently has rarely, if ever, occurred.

Ryder¹³ stated that his own brought the total number of authentic cases to 123. It is the purpose of this report to raise that total by one.

Case Report

On January 28, 1944, Mrs. J. L., a 29-year-old para vii, gravida viii, was admitted in active labor with strong pains. Last menses began April 16, 1943, and lasted six to seven days, and she claimed that fetal movements were first felt during the sixth month of gestation.

Twenty-five minutes after admission, the membranes became visible and she was moved to the delivery room. As she was placed on the delivery table, a membrane-covered mass protruded from the vagina. The membranes ruptured spontaneously, and a loop of umbilical cord about 30 cm. in length was found prolapsed. Shortly thereafter, the infant was heard crying loudly enough to be heard by all in the room. The mother, thinking that the baby had been delivered, asked, "Is it a boy or girl?" To her amazement, she was informed that the child had not been born. At the time, fetal heart tones were 100 per minute but were still strong.

Vaginal examination revealed the cervix dilated 6 to 7 cm., cephalic presentation, with the umbilical cord compressed between the fetal head and the superior rim of the cervix. An unsuccessful attempt was made to replace the loop of cord, and it was decided to deliver by version and breech extraction.

Two fingers were inserted as a bridge over the strangulated umbilical cord, and the cervix allowed to dilate. The fetal heart tones were now reduced to 90 per minute and were somewhat irregular. Immediately before delivery, the fetal heart tones were not heard, but it was deemed advisable to continue with the procedure, with the hope of resuscitating the child.

Without unusual difficulty, a female stillborn which weighed 6 pounds, 2 ounces was delivered by combined podalic version and breech extraction. To prevent infection, the mother was given an intrauterine douche with $\text{KMnO}_4\text{-H}_2\text{SO}_4$ solution.

The mother had a temperature of 101.2°F . six hours post partum, but it subsided the same day. The puerperium was otherwise uneventful. The patient signed a release and was discharged on the ninth postpartum day.

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AN ANTEPARTUM STUDY OF FETAL POLARITY AND ROTATION*

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VOLUMINOUS statistics on the frequency of fetal presentations and positions in a large series of cases have been reported in the past and are available in obstetric texts. Most observers have agreed that vertex presentations occur with 95 to 96 per cent regularity, breech presentations with 3 per cent frequency, and face and transverse making up the total. Since the diagnosis of presentation and position depends upon *the time that the diagnosis is made*, much of the labor spent in compiling such statistics was wasted since no standard timing measures were used. Moreover, in most of the earlier studies discrepancies must have occurred frequently since the diagnosis of presentation was made solely on a basis of physical examination without the aid of x-rays.

With the advent of modern roentgenology and the concurrent simplification of radiologic apparatus and technique, much more accurate obstetric diagnoses are being made, and a better foundation of intrauterine physiologic activity of the fetus is being evolved.

While most obstetricians still consider breech presentations eutocia (notwithstanding the trebled fetal mortality, and the greater maternal morbidity from sepsis and lacerations resulting from such deliveries in the hands of the general practitioner who still does most of the general obstetrics), this author believes with DeLee and others that breech presentations should be considered dystocia.

In this respect, exact information relative to such errors in fetal polarity, and the resulting natural and scientific efforts of accommodation and adjustment by rotation and version are of great value. Accordingly, a radiologic antepartum study of fetal polarity from the time when the fetal parts first become visible until just before delivery was considered desirable. This study could only be of value if each individual pregnancy was carefully studied and followed and the progress recorded. The utilization of a pregnancy series of such a magnitude as to become unwieldy and render roentgen observations sporadic and haphazard was at once dismissed in favor of a more carefully controlled smaller group of cases.

Procedure

One hundred unselected primiparous women were studied by ordinary palpatory methods and by x-ray visualization from early pregnancy until term. X-rays of the fetus were taken as early as

*This study was completed before entering the United States Public Health Service. The opinions and assertions contained herein are the private ones of the writer, and are not construed as official, or reflecting the views of the U. S. Public Health Service.

radiopaque shadows could be detected and at regular intervals during the gestation. Plates were exposed at about the fifth month of pregnancy (eighteenth to twenty-second week), the seventh month (28 to 30 weeks), the eighth month (32 to 34 weeks), and approximately a week or so just prior to the expected date of delivery (37 to 39 weeks). Pelvimetry and cephalometry studies were also made just before delivery.

From the accompanying table it will be seen that at approximately five months of pregnancy, 74 cases were cephalic presentations, and 26 were not in the normal polarity (normal polarity being a parallelism of the fetal axis with the long axis of the patient, the cephalic pole presenting at the inlet). Repeated observations of the 74 cephalic presentations at the intervals indicated above revealed no change in presentation throughout the entire course of gestation. Although DeLee cited a case which changed from a cephalic presentation lodged deeply in the pelvic excavation to a breech presentation late in pregnancy, such an occurrence is probably a rarity; and reports of such rotations should be supported by x-ray evidence. On the other hand, it is commonly accepted that changes in fetal position are variable and frequent, and the x-rays of this series support this view without question.

Closer scrutiny of the 26 cases with errors in polarity reveals interesting changes. Two of these had been found to be in the transverse presentation at five months of pregnancy. By the end of the seventh month these two fetuses had rotated to become vertex presentations and remained so until delivery. In addition, 16 of the remaining 24 breech presentations had rotated to cephalic presentations in the same period of time. At the end of the eighth month of gestation, one more breech had rotated to vertex but seven remained in the breech presentation deeply placed in the pelvic cavity.

TABLE I. SERIAL X-RAYS OF THE ABDOMEN DURING THE COURSE OF PREGNANCY STUDIED FOR CHANGES IN FETAL POLARITY

| | 5TH MONTH (18 TO 22 WEEKS) | 7TH MONTH (28 TO 30 WEEKS) | 8TH MONTH (32 TO 34 WEEKS) | ONE WEEK BE- FORE TERM (37 TO 39 WEEKS) |
|-------------------------|----------------------------------|----------------------------------|----------------------------------|---|
| Cephalic presentation | 74 | 92 | 93 | 99 |
| Breech presentation | 24 | 8 | 7* | 1 |
| Transverse presentation | 2 | 0 | 0 | 0 |

*After the completion of eight full months of gestation, seven pregnancies remained in the breech position deep in the pelvic excavation. Six of the seven breech presentations were rotated manually to vertex by external version at this time, and one breech allowed to continue to term since an elective low-flap cesarean section was to be done in this instance for another indication.

At this time external versions were performed on six of the remaining seven breech cases, and x-rays taken subsequent to the versions showed cephalic presentations.* These six cases continued along as vertex presentations and were delivered as such. The remaining case in which no version was attempted was allowed to remain in the breech state until one week before term when a planned elective cesarean section (low flap) was performed for cervical fibroid blocking the passageway. The fetus was delivered easily by podalic extraction at operation.

*It is not within the province of this short paper to discuss the advantages and disadvantages of external version. However, one fact must be stated at this time which is entirely relevant. Unless the exact position of a breech, or transverse presentation is outlined by x-rays, and the proper application of the laws of physics applied in making pressure on the fetus in utero, the results of external version will be sadly disappointing. A thorough study of external version will be presented in a subsequent paper.

Summary

Radiographic antepartum polarity studies were made at periods throughout the course of pregnancy in 100 unselected primiparous women. At five months of gestation, 74 cephalic presentations were found and 26 errors in polarity were disclosed (24 breech and two transverse). After 8 months of pregnancy, 19 of the 26 faulty presentations had rotated spontaneously to cephalic presentation. At this time 6 of the remaining 7 breech cases were rotated by external version, while the remaining breech presentation was allowed to go to term as a breech in view of the planned elective cesarean section (low flap) for cervical fibroid blocking the passageway. At term 99 per cent of the cases were normally delivered as vertex presentations, and the one child delivered by podalic extraction in the course of the elective cesarean operation.

Conclusions

Repeated radiologic studies during the course of pregnancy are a valuable method of learning the exact intrauterine changes in polarity of the fetus.

Up to one month prior to delivery, 73 per cent of errors of polarity (breech and transverse presentations) will rotate spontaneously to the cephalic presentation.

If by eight full months of gestation spontaneous version has not occurred, it is suggested that external version be attempted to effect a normal polarity, since at this stage with the breech deep in the pelvis spontaneous version is unlikely.

Of 100 primiparous women who presented radiologic evidence of 26 errors in polarity early in pregnancy, 99 per cent were finally delivered normally with the vertex presenting. One breech which did not rotate by the eighth month was allowed to continue to term as such, since an elective cesarean section was to be performed for another indication.

HYPERTHYROIDISM AND PREGNANCY

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MOST authors agree that hyperthyroidism is a comparatively infrequent complication of pregnancy. Portis and Roth¹ showed an incidence of 1.4 per cent, while Javert² reported 0.076 per cent. In the Bronx Hospital, over a period of six years, 15,864 pregnant women were admitted. Of these, only 12 or (0.075 per cent) showed abnormal hyperactivity of the thyroid gland. These cases were divided clinically, into diffuse exophthalmic goiter (3 cases), toxic adenoma (1 case), and hyperthyroidism (8 cases). The symptoms of hyperthyroidism developed during pregnancy in 7 cases, antedated the pregnancy in 3 cases, while 2 cases dated their symptoms to a previous pregnancy.

Of the 12 patients with hyperthyroidism, 8 went to term, 1 had operative interference in her thirtieth week of gestation, and 3 aborted. Of the 3 abortions, two cases were performed for therapeutic reasons, on a cardiac basis. One of the therapeutic abortions was performed on a patient with a history of cardiac collapse during her last delivery. The other therapeutic abortion was started by x-ray, on a class iii cardiac near menopause; but had to be completed by operative measures a month later because of bleeding. One patient aborted spontaneously in her fifth month of gestation, six weeks following a subtotal bilateral thyroidectomy.

There were 9 multiparas and 3 primiparas; and the average age was 30.9 years.

Toxemia of pregnancy was observed in 5 cases (or 55.5 per cent) of the cases reaching viability or term.

The average basal metabolic rate of plus 40 per cent was reduced by hospitalization to an average of plus 23 per cent.

The type of delivery revealed seven (or 77.7 per cent) spontaneous deliveries. Two were operative deliveries, one a midforceps, and the other a Voorhees' bag, followed by version and breech extraction for central placenta previa.

Subtotal bilateral thyroidectomy was done in four cases, three during pregnancy, and one 4½ months following delivery. The first patient, operated on at the end of her second month of her pregnancy, had a spontaneous abortion 2½ months later. The second patient was thyroidectomized in her third month of gestation, went to term, and delivered spontaneously of a Mongolian idiot. Interestingly enough, in her previous pregnancy, she also delivered a Mongolian idiot. The third patient had a therapeutic abortion done at the end of the second month of a previous gestation. She promptly became pregnant two months later, and her symptoms became aggravated. This time she had a subtotal thyroidectomy near the end of her third month of gestation,

and then delivered spontaneously at term. The fourth case is now presented in more detail.

Case Report

Patient B. D., aged 39, was a gravida ii para i. Her last menstrual period was July 28, 1940, and her expected date of confinement was May 5, 1941. She was admitted to the Bronx Hospital on February 16, 1941, because of painless bleeding, 2½ months before term.

Past History.—Five years previously, she had a normal spontaneous delivery of an eight months' premature baby, that is living and well. Three years ago, she came to her family doctor because of a relative sterility, and on examination, was found to have hyperthyroidism with a basal metabolic rate of plus 60 per cent. Operation was suggested, but the patient refused.

She was given iodides, with a reduction of her basal metabolic rate to plus 48 per cent. Iodides were continued and seemingly controlled the severe symptoms of her hyperthyroidism. In July of last year, she became pregnant. At that time, her blood pressure was 135 systolic over 80 diastolic, with a blowing systolic at the right base of the heart. The pelvic measurements were ample. During her prenatal course, the blood pressure varied from 135 systolic over 80 diastolic to 150 systolic over 100 diastolic, with the urine consistently negative.

Present History.—Patient began to stain two weeks before admission to the hospital, for which she was kept in bed. On February 15 the day before admission, she had active bleeding for a short while. The following day, she bled profusely and was told to come to the hospital immediately.

On admission, the red blood count was 3½ million with 78 per cent hemoglobin. Slight bleeding was present. The patient was typed and the donor ordered to be ready. The height of the fundus was three fingers above the umbilicus. No fetal heart was heard.

Vaginal examination revealed a vertex presentation, the cervix 1½ fingers dilated, and the presence of a central placental previa.

Because it was scarcely likely that the fetus was viable, cesarean section was considered not indicated, first, because of the period of gestation, and secondly, the character of the bleeding. Under light anesthesia, a No. 4 bag was readily introduced into the cervix in front of the placenta, without any additional bleeding, and the vagina was packed with iodoform gauze. Sedation and a transfusion of 500 c.c. of citrated blood was given. The patient was watched all night for bleeding and other physical signs, with the pulse and blood pressure taken at frequent intervals.

The next morning the bag was in the vagina and the cervix was four fingers dilated, and readily dilatable. The edge of the placenta was approached to the patient's left, and separated. The membranes were then ruptured. The posterior foot was grasped, and an internal podalic version and extraction was performed, with delivery of a stillborn female, weighing 3½ pounds. The placenta followed the head as it was delivered. The uterus and the vagina were packed with fifteen yards of iodoform gauze, which was removed in forty-eight hours.

One-half hour following the patient's removal to her room, her pulse suddenly rose to 180. There were extreme restlessness, marked flushing, and an anxious facies. Her blood pressure was 140 systolic over 0 diastolic. No diarrhea, no jaundice, and no mental symptoms were present. Medical consultation suggested we were dealing with a thyroid

storm, and advised, (1) sedation, (2) 1,000 c.c. of 10 per cent glucose intravenously with sodium iodide or Lugol's solution added, (3) oxygen inhalation, and (4) cold packs or ice bags to head and body. These instructions were followed.

The following day, the temperature ran up to 103° F., but gradually came down to normal in the next four days, with the pulse gradually slowing to 100.

She was discharged on the tenth day post partum with the hyperthyroidism apparently under control, the temperature normal, the pulse rate 90, and the general condition good. Since leaving the hospital, her basal metabolic rate rose to plus 60 per cent. Four and one-half months later, she re-entered the hospital and had a subtotal bilateral thyroidectomy performed. At her last visit, one year later, patient was in excellent condition.

Discussion

Bothe³ showed the experimental evidence of the relation of the anterior pituitary hormone to the activity of the thyroid gland, whose function is the production of a secretion which activates heat and energy production by regulating the rate of oxidation in the cells throughout the body. Mussey⁴ states that the thyrotropic hormone of the anterior lobe of the pituitary stimulates the thyroid gland to hyperplasia and the production of thyroxin, and causes the release of stored colloid. Overproduction of thyroxin tends to develop an antihormone in the body, which depresses the thyrotropic output of the anterior lobe of the pituitary. The thyrotropic content of the pituitary, therefore, becomes inversely proportional to the thyroxin output of the thyroid gland. Sufficient iodine is also necessary to enable the thyroid gland to discharge all the thyroxin it produces. If the amount of ingested iodine is insufficient for the physiologic demand of the increased metabolism during pregnancy, the appearance of colloid or simple goiter may result. This result may be hypothyroidism in the mother, and if the degree of hypothyroidism is sufficient, it may cause miscarriage or the development of colloid goiter or cretinism in the infant.

On the other hand, if there is a sustained stimulation of the thyroid in conjunction with certain unknown factors, a condition of hyperthyroidism develops. This may occur during pregnancy, or more commonly the woman may become pregnant while the hyperthyroidism exists. Occasionally, cases of what was thought to be toxemia of pregnancy have turned out to be the result of an overactive thyroid gland. Javert, however, states that the high incidence of toxemia of pregnancy (76 per cent) in his series of hyperthyroidism in pregnancy seems significant, and raises the question of a common factor in toxemia and in thyrotoxicosis.

The diagnostic features of hyperthyroidism in pregnancy are practically identical with those of hyperthyroidism in the nonpregnant state. But the subsequent course frequently assumes a different clinical picture. The majority of patients show either a stationary condition, or an amelioration of symptoms, and only a small number show a progression as the gestation continues.

With regards to treatment, all authors agree that it is the thyrotoxicosis and not the pregnancy which should be interrupted. Therapeutic abortion is not indicated, except in rare instances, as in Portis and Roth's case, where multiple operations on the thyroid precluded the likelihood of a further successful operation. Mild hyperthyroidism complicating pregnancy may be controlled by medical management. The use of iodine early in pregnancy has reduced the incidence of hyperthyroidism. If the medical treatment does not produce the proper result, Bothe, Mussey, and Portis and Roth advocate surgical interference on the thyroid, regardless of the period of gestation. Javert, however, feels that with proper treatment patients with hyperthyroidism may safely go through a pregnancy and sometimes even be benefited thereby. Hospitalization for evaluation and stabilization may be necessary several times during the antepartum course. As a general rule, he feels the best time for operation on the thyroid, is in the first postpartum year, so that the effects of pregnancy on the thyroid gland are no longer present. He does admit, however, that thyroidectomy may be performed in individual cases.

Conclusions drawn from these comments seem to indicate that each case should be individualized. If possible, the pregnant woman with hyperthyroidism should be carried to term, and only exceptional cases, that grow progressively worse, in spite of adequate and intensive medical treatment, should be thyroidectomized. It should be a dictum that the pregnancy itself should not be interfered with, unless there is an obstetric reason.

Summary

1. There were 12 cases of hyperthyroidism in 15,864 pregnant women, an incidence of 0.075 per cent.
2. Therapeutic abortions were done in 2 cases, an incidence of 16.6 per cent.
3. There were 9 multiparas and 3 primiparas, with an average of 30.9 years.
4. Toxemia of pregnancy was observed in 5 cases, or 55.5 per cent of the cases reaching viability or term.
5. The average basal metabolic rate of plus 40 per cent was reduced by hospitalization to an average of plus 23 per cent.
6. Subtotal bilateral thyroidectomy was done in 4 cases, an incidence of 33.3 per cent.
7. A severe case of hyperthyroidism during pregnancy, complicated by a central placenta previa, is presented.
8. Pregnancy and hyperthyroidism are discussed.

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HEMORRHAGE AS THE MOST IMPORTANT CAUSE OF MATERNAL DEATH IN BROOKLYN, CITY OF NEW YORK

An Analysis of the Puerperal Deaths of 1943*

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IN THE course of our inquiry into the circumstances of every maternal death in Brooklyn, we have reviewed at monthly meetings, to which all physicians are invited, those cases which appear to teach valuable lessons to general practitioner and obstetrician alike. In 1937, and for a short time thereafter, we discussed every death, and clearly our intention was to assign preventability and fix responsibility. This practice was abandoned partly because we could not agree upon the criteria of preventability, but largely because we became aware of the enormous educational value of the common obstetric conference. Those who attend these meetings will testify to their teaching value. It is true that interest has never been what it might be, since the general practitioner group has always been poorly represented, unconvinced that group discussion of actual cases of maternal death is a worth-while method of learning. Yet, what could be better or easier? Widespread knowledge of the principles of obstetric practice is vital, if the problems which confront us every day are to be solved rightly. True, the art of obstetrics cannot be taught by round table discussion any more than it can be learned from a textbook, yet discussion of the details and implications of maternal deaths can readily be converted into reduced mortality.

Once every year, a complete case study is presented to the medical profession at an open meeting of this Society. I believe that we have developed a simple method of postgraduate education which, if fully effective, should prove to be highly developed preventive medicine. Our puerperal mortality experience is good, and I like to feel that we have helped to reduce the death rate, yet perhaps we are but participating in the extraordinary decline in puerperal death rates going on in no less than forty-one states.

In the United States during 1942,¹ the latest year for which figures are available, the number of live births increased 11.8 per cent, yet the number of puerperal deaths decreased from 7,956 in 1941 to 7,267. The national maternal death rate was 2.6 per 1,000 live births, the lowest rate yet recorded.

Through the personal interest of Mr. Thomas J. Duffield, Director of the Bureau of Records and Statistics of the Department of Health, City of New York, figures for Brooklyn for 1943 have been tabulated at this early date, and transcripts of death certificates sent us throughout the year have been checked by the Visiting Nurse Association of Brooklyn.

The number of live births occurring in Brooklyn during 1943 was 49,423, and the total number of births was 52,352. The puerperal rate based on 55,660 reported terminated pregnancies and standardized for color, on the basis that each borough had the same proportion of colored

*Read at a meeting of the Brooklyn Gynecological Society, May 5, 1944.

pregnancies as the city as a whole is 20.3. This rate for the entire City of New York is 20.1. In 1942, the Brooklyn rate was 20.7. If this rate were computed on the basis of live births, as is the national figure, the rate would be 22.7. The rate, however, is not a true measure of the risk of pregnancy, for deaths from abortion are included, while pregnancies terminating in abortion are not.

In 1943, 121 women died of causes associated with pregnancy and childbirth; 9 of these deaths were assigned to nonpuerperal causes, and 112 cases were assigned primarily to puerperal causes. In the puerperal group of 112 cases, 101 women were white and 11 colored.

Nonpuerperal Causes of Death (9)

It is not generally appreciated that preventive programs cannot be planned without consideration of the nonpuerperal causes of death, primary as well as secondary. Nephritis was assigned as the cause of death in 4 cases, yet in one of these, death was really due to eclampsia and cesarean section. In 2 cases, death was due to severe cardiac disease; both women died undelivered without any prenatal care whatever; one was found moribund at home, and the other died shortly after admission to the hospital.

Cardiac Disease.—Among the secondary nonpuerperal causes of death, cardiac disease was reported in 17 cases, but in not all of these was it actually present. In certifying obstetrical death, mention of circulatory failure, vasomotor collapse, cardiac decompensation, heart failure, acute cardiac dilatation and acute or chronic myocarditis unduly weights statistics with faulty figures, for the vital statistician will assign death to heart disease. In one case, for example, ascribed to acute myocarditis, death was due to severe postpartum hemorrhage which followed unattended delivery of a woman who had been long in labor. In another case where the patient was found in shock, with bed linen soaked with blood, two hours after delivery, death was said to be due to "postpartum hemorrhage and cardiac decompensation."

Death was due to subacute bacterial endocarditis in 4 cases. In one case death followed home delivery in the fifth month. In another case the death certificate was well written: "Subacute bacterial endocarditis, streptococcus viridans, secondary to rheumatic heart disease. Contributory: pregnancy 5½ months; embolism from heart to brain; left hemiplegia." These deaths were assigned to puerperal causes.

In 3 cases associated with operative delivery, heart disease contributed to death. The sequence of events is stated:

CASE 1.—Mitral stenosis, decompensated one week before admission to the hospital with membranes ruptured 48 hours; dyspnea grew worse and pulse rate rose to 140. She was not in labor. Under spinal anesthesia, the cervix was dilated manually, and she was delivered with forceps; postpartum hemorrhage; death during transfusion.

CASE 2.—Primigravida with severe heart disease, excellent prenatal care, had not decompensated during pregnancy. Elective cesarean section at term under caudal anesthesia; death from heart disease one day later.

CASE 3.—Para ii, who had refused to enter the hospital several times during pregnancy, was delivered spontaneously in the hospital after quick labor. Death in heart failure 5 days later.

Pre-eclampsia and eclampsia complicated serious cardiac disease in 2 patients delivered by cesarean section; death from heart disease weeks later.

In addition to the 2 deaths assigned primarily to heart disease, 3 more young women, who had no prenatal care, died of cardiac disease during the last trimester. One died at home after delivering herself unattended; and 2 others who were admitted to the hospital in heart failure, died of hemorrhage.

Heart disease played an important part in the deaths of 13 women, or 10 per cent of the total number of 121 deaths associated with pregnancy and childbirth.

Pelvic Tumors.—Fibroids and ovarian tumors were associated with death in 5 cases. Brief data indicate controllable factors:

CASE 1.—Multiple myomectomy during laparotomy for ruptured ectopic gestation was followed by peritonitis.

CASE 2.—Cesarean hysterectomy for fibroids and an endometrial cyst were followed by wound disruption and peritonitis.

CASE 3.—Myomectomy in the course of classical cesarean section was followed by intestinal obstruction.

CASE 4.—Cesarean section with removal of an ovarian teratoma discovered 5 hours after onset of labor was followed by pulmonary embolism 12 days post partum.

CASE 5.—An ovarian cyst found after 14 hours of labor was readily removed at laparotomy, and delivery then easily effected with forceps. Death was due to secondary hemorrhage from the tumor pedicle.

Puerperal Deaths (112)

The official tabulation of all the deaths assigned to puerperal causes follows: (See Table I.)

TABLE I. CAUSES OF HEMORRHAGE

| NUMBER | CAUSES | PRIMARY | SECONDARY |
|--------|--|---------|-----------|
| 140 | Abortion with infection | 10 | |
| 141 | Abortion without infection | 9 | 2 |
| 142 | Ectopic gestation | 9 | |
| 143 | Hemorrhage of pregnancy | 1 | |
| 144 | Toxemias of pregnancy | 4 | 2 |
| 145 | Other diseases and accidents of pregnancy | 4 | 3 |
| 146 | Hemorrhage of childbirth | 20 | 2 |
| 147 | Infection | 21 | 1 |
| 148 | Puerperal toxemias | 14 | 4 |
| 149 | Other diseases and accidents of childbirth | 11 | 22 |
| 150 | Other unspecified | 9 | |
| | Total | 112 | 36 |

Comparison of the major causes of death with those of the preceding year is made below: (See Table II.)

TABLE II. COMPARISON OF MAJOR CAUSES OF DEATH
1942 AND 1943

| RUBRIC | CAUSES | 1942 | 1943 |
|-------------|---------------------------------|--------|--------|
| 140 and 141 | Abortion | 21 | 19 |
| 142 | Ectopic | 6 | 9 |
| 143 and 146 | Hemorrhage | 15 | 21 |
| 144 and 148 | Toxemia | 24 | 18 |
| 147 | Infection | 27 | 21 |
| 145 and 149 | Accidents | 14 | 15 |
| 150 | Other | 7 | 9 |
| | Number of puerperal deaths | 114 | 112 |
| | Reported terminated pregnancies | 56,247 | 55,660 |
| | Rate | 20.7 | 20.3 |

Deaths in Early Pregnancy

Abortion.—Abortion was responsible for 19 deaths, or 17 per cent of all the deaths from puerperal causes. This is approximately the same as the national rate. In the infection group, nearly all were induced. Deaths from toxemia, hemorrhage and trauma which occur before the twenty-eighth week of gestation (7 lunar months) are not assigned to their specific causes, but to abortion. Two cases will illustrate:

CASE 1.—History of hypertension for three years; aged 24; no prenatal care. Admitted to hospital with blood pressure 220/160 and blurring of vision. Abdominal hysterotomy under general anesthesia was followed by hemorrhage and shock; death from septicemia 3 weeks later.

CASE 2.—Multipara, in the sixth month of pregnancy, was admitted to the hospital in profound shock following profuse hemorrhage due to ablatio placentae. Morphine and plasma were administered promptly, and the membranes were artificially ruptured. Delivery expedited by pituitrin was rapid, and she received 750 c.c. of blood following expulsion of the placenta. Her condition improved markedly, but she died of pulmonary edema a week later.

In the absence of cardiac disease, hemorrhage caused death in early abortion. One case is interesting.

CASE 1.—Bleeding profusely, a patient was admitted to the hospital in profound shock. After a 3 months' placenta had been removed from the cervix, bleeding ceased. She received plasma and two blood transfusions, but died 9 hours later, blood pressure never rising above 60/40.

There were 5 deaths in the abortion group directly due to hemorrhage and shock, and 3 more in which profuse hemorrhage was reported.

Ectopic Gestation.—There were 9 deaths from ectopic gestation, while there were 6 in 1942, and only 3 in 1941. The optimum time for operation passed in 6 cases due to long delay in diagnosis. Two patients admitted to the hospital in severe shock were not operated upon, one living for three hours without any improvement after large transfusion. In another case peritonitis followed incidental multiple myomectomy. And in one case death occurred as a result of spinal anesthesia while the peritoneum was being opened.

Toxemia

As hitherto, in no case did toxemia or eclampsia fail of mention on the certificate of death. All our experience has been to the contrary in the case of infection, and in hemorrhage particularly. The number of deaths was less than in 1942, but more than twice as great as in 1941.

In the total number of 24 cases in which toxemia was mentioned, 5 cases were found in which this diagnosis does not appear to be warranted. In 9 cases of eclampsia, 3 women died undelivered, and 2 were subjected to cesarean section after the onset of convulsions. With notable exceptions, inadequate or no prenatal care as well as formidable operative procedures were common, yet as might be expected, excellent prenatal care and spontaneous delivery did not prevent death. Shock occurred in some cases without trauma or undue loss of blood.

To illustrate the importance of good prenatal care and the influence of hard delivery upon the outcome, the salient facts in certain cases of pre-eclampsia are briefly cited.

CASE 1.—Admitted to hospital with blood pressure 226/110 and history of severe bleeding in the seventh month. At term, her complaints of blurred vision, headache and vomiting were ignored until she became stuporous, and neighbors called an ambulance.

CASE 2.—Classical cesarean section after 90 hours of labor with membranes ruptured; death from peritonitis.

CASE 3.—Primigravida 3 days in labor; failure of midforceps and forceps rotation; craniotomy; shock.

CASE 4.—Primigravida induced by rupture of membranes; after 12 hours of labor, cervical incisions under general anesthesia taken very badly, hemorrhage and shock; uterus packed. Cardiac stimulants, adrenalin, and several doses of ergotrate without control of bleeding; no transfusion.

Infection

In the group of 21 cases assigned to infection, it is of particular interest that 11 cases of pulmonary embolism are included. Cesarean section contributed to death in 8 cases. In 3 cases said to be due to pulmonary embolism, death was due to general anesthesia (1 case), massive retroperitoneal hemorrhage following lower segment cesarean section (1 case), and rupture of the uterus (1 case). In all but 2 cases, death occurred late, from the twelfth day to fourteen weeks post partum.

Cesarean Section

Cesarean section contributed to death in 30 cases, 27 per cent of the total number of puerperal deaths, or 36 per cent of the deaths, if abortion and ectopic gestation are excluded. In 9 cases, death was assigned to this cause, and to other causes in 16 cases as follows: hemorrhage (6), infection (7), toxemia (2), and nephritis (1). There were 5 additional cases in which this operation was reported and not tabulated, other causes receiving preference. In 2 cases of cesarean hysterectomy death was due to wound disruption and peritonitis. One case in which cesarean section had been planned, but the uterus found to be ruptured is not included.

In 11 cases, there had been no labor. In 6 elective operations performed because of previous cesarean section, death was due to peritonitis (1 case), massive pulmonary collapse (1 case), and hemorrhage (4 cases). An example follows:

CASE. After elective lower segment operation under general anesthesia, the patient was returned to her bed in shock. Bleeding continued for five hours. Transfusion, attempted several times, was successful for only 300 c.c. of blood.

The lower segment operation was performed after labor of 48 hours (2 cases) and 72 hours (1 case) and in one case classical cesarean section was performed after 90 hours of labor. In several cases, intraperitoneal and intravenous chemotherapy was administered.

In the entire group of 30 cases hemorrhage was severe or caused death in 11 cases, though general anesthesia was a contributory cause in 3 of them. Death was due to infection in 9 cases. In 2 cases death attributed to infection was reassigned to hemorrhage. For example:

CASE 1.—Cesarean section for placenta previa after profuse bleeding at home. Shock occurred during removal to bed. Plasma and intravenous glucose were administered. Death from peritonitis fifteen days later.

Hemorrhage

By this time it has become clear that a "broad stream of blood" runs through these statistics. Officially 21 cases were assigned to hemorrhage. Repeated antepartum hemorrhage at home, placenta previa and ablatio, long labor, unrecognized transverse presentation, postpartum hemorrhage, retained placenta and ruptured uterus are included. Incision or manual dilatation of the cervix, version and extraction, forceps, craniotomy and even episiotomy and spontaneous delivery are reported in this group.

In some cases proper shock therapy was prompt though ineffective, probably because shock had existed too long before admission to the hospital. In a great many cases, plasma, glucose solutions, cardiac stimulants or comparatively little blood, often very late, were relied upon for replacement of lost blood. In many cases the uterus was packed, yet bleeding did not stop. And sometimes consultants gave strange advice.

Space will not permit even a brief report of all the cases in this group, though every case is highly instructive. A few will suffice.

CASE 1.—Unattended delivery after 24 hours of labor was followed by profuse hemorrhage. After the placental stage, the uterus repeatedly relaxed. Intravenous glucose therapy was attempted, but veins could not be entered. Death from shock in one hour.

CASE 2.—Para xv, no prenatal care, delivered herself at home. One hour later she was found in profound shock.

CASE 3.—Following profuse hemorrhage at home from placenta previa, patient entered the hospital exsanguinated with a pulse of 160. She was given morphine, 500 c.c. of plasma, 2,000 c.c. of glucose solution and cesarean section was rapidly performed under ether anesthesia. Her condition was poor throughout, so she was transfused with 500 c.c. of blood immediately afterward, hemorrhage continuing. Profuse hemorrhage followed removal to bed.

CASE 4.—Ten days post partum, after sudden hemorrhage estimated at 1,000 c.c., blood pressure fell to 84/46, and 500 c.c. of blood were administered. Examination showed a dilated cervix and retained tissue. During its removal, two days later, profuse hemorrhage recurred. Vaginal packing and 500 c.c. of blood followed. Upon removal of the packing the next day, profuse hemorrhage estimated at 800 c.c. occurred. Then 1,000 c.c. of plasma and 750 c.c. of blood did not save her.

CASE 5.—Spontaneous delivery followed by profuse post-partum hemorrhage. Saline and plasma were administered. One hour later, it was thought that her condition would not permit removal of the placenta. Death one hour later with placenta retained.

In case reports hemorrhage was so commonly encountered, that it would appear to be wise and necessary to revise official figures in order to learn its true importance. Shock is not included in this revision unless hemorrhage was mentioned. Nor are cases with blood loss said to be 500 c.c. included; nor any case unless hemorrhage was reported as severe or profuse. Nor is a patient with severe leucemia who died from severe postpartum hemorrhage from the genital tract as well as from her nose and throat, or 2 women with severe anemia who had no undue bleeding, yet died of shock shortly after delivery. Deductions for hemorrhage are made in the following table. (See Table III.)

Obstetrical death is commonly the result of several causes, rarely one, and actually it is very often impossible to assign death to one cause.

TABLE III. HEMORRHAGE AS A CONTROLLABLE FACTOR

| RUBRIC | CAUSES | CAUSES AS OF CERTIFICATE OF DEATH | HEMORRHAGE FACTOR AS OF CASE REPORTS |
|----------|------------|---|--|
| 140, 141 | Abortion | 19 | 8 |
| 142 | Ectopic | 9 | 9 |
| 143, 146 | Hemorrhage | 21 | 21 |
| 144, 148 | Toxemia | 18 | 4 |
| 147 | Infection | 21 | 8 |
| 145, 149 | Accidents | 15 | 8 |
| 150 | Other | 9 | 2 |
| | Total | 112 | 60 |

The accuracy and value of statistical deductions depend upon the quality of the information furnished by the certificates of death. Dunn² says, "The cause of death information given on the death certificate is, for the most part, fairly reliable. . . . Although a number of notable studies have been made on the accuracy of medical diagnoses, there is an unfortunate lack of national statistics on the subject. All of these investigations are extremely limited in scope, since they are based upon comparisons of autopsy and clinical records in certain hospitals."

Numerous controllable factors are indicated in this study. The scope of this paper will not permit discussion of the importance of proper application of the basic concepts of good obstetric practice. Certainly casual obstetricians should not make weighty decisions thoughtlessly or hastily, nor should they attempt operative procedures beyond their skill without consultation or assistance. That those upon whom they lean for advice and support should be well qualified, is obvious.

Though many women in Brooklyn seek no prenatal care at all, it is still true that not every physician realizes the importance of pre-eclampsia, and the necessity of hospitalization for its observation and treatment. Nor are we all convinced of the gravity of the association of heart disease and pregnancy, and of the need for continuous hospital care, no matter how long, after cardiac decompensation.

Every obstetric patient should have her blood typed, with determination of her Rh factor, early in pregnancy, perhaps at the time blood for her Wassermann test is taken.

If only for its own good, every hospital should insist upon observance of good rules for consultation in obstetric emergencies. And the hospital should see to it that facilities for blood transfusion are satisfactory. It is true that plasma has been made more generally available, yet more and more, it becomes apparent that plasma will not save life if blood loss has been great. Undue confidence is had in plasma. Our Brooklyn hospitals need blood badly. It is our hope that the American Red Cross will lend us a helping hand.

In Brooklyn, hemorrhage is the outstanding controllable factor in maternal mortality. We became acutely aware of this in 1940,³ and it has been so ever since.^{4, 5} In 1943, it was a significant factor in 53.6 per cent of all our puerperal deaths. Its importance cannot be overestimated. Our experience, as of our own figures, as shown in the following table. (See Table IV.)

Reviewing the maternal mortality statistics of the United States for 1941, Yerushalmy⁶ points out that "Infection was the leading cause of death (3,034—38 per cent) while the other two major groups of causes were each responsible for one quarter of the maternal deaths. Hemor-

TABLE IV. MAJOR CAUSES OF MATERNAL DEATH
BROOKLYN 1937 TO 1943

| YEAR | INFECTION | TOXEMIA | HEMORRHAGE |
|-------|-----------|---------|------------|
| 1937 | 27 | 26 | 29 |
| 1938 | 27 | 18 | 27 |
| 1939 | 30 | 12 | 14 |
| 1940 | 18 | 10 | 28 |
| 1941 | 10 | 8 | 20 |
| 1942 | 25 | 22 | 30 |
| 1943 | 13 | 14 | 60 |
| Total | 150 | 110 | 208 |

rhage, trauma or shock was the cause of 2,032 of the maternal deaths, and toxemias were responsible for 2,031.

If the national figures for these three great causes of death in 1942 are compiled in exactly the same way, we find that the number of deaths from infection was 2,618, from toxemia 1,807, and from hemorrhages 2,018. The percentage reduction in infection was 10 per cent, in the toxemias 11 per cent, and in the hemorrhage group only 0.005 per cent. This resistance of hemorrhage is of great significance.

For these national figures it must be understood that only certificates of death were available, and in a great many of these, the basic data were so meager that little more than the fact of pregnancy could be established.

It has been said over and over again, that infection as the most common cause of death is the most important. Definitely the outstanding controllable factor in Brooklyn, hemorrhage is no doubt far more common everywhere than indicated by its statistical frequency. Preventive measures for reduction of maternal mortality will produce greater results, if emphasis is placed on hemorrhage, rather than infection. At present, hemorrhage is the most important cause of maternal death, and probably the most common as well.

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32 REMSEN STREET

Department of Reviews and Abstracts

WEIGHT CHANGES AND WATER BALANCE IN NORMAL AND TOXIC PREGNANCY

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W EIGHT changes in pregnancy have been extensively studied because many investigators have felt that excessive gains in weight are correlated with certain complications of pregnancy, parturition and puerperium, especially with late toxemia (pre-eclampsia and eclampsia). In reviewing the literature, one finds that what is essentially a statistical problem has very seldom been subjected to statistical operations other than to determine the average weight change in relation to the incidence of the complication (s) under analysis. Furthermore, the data given are usually so few as to preclude any analysis by the reader. Curiously, the *average* gain is frequently calculated and then implicitly taken as the *upper normal*, thereby negating the normality of half the normal series from which the average was determined.

Weight Changes in Normal Pregnancy

There have been four approaches to the problem as to what constitutes normal weight change in pregnancy. 1. The average change during normal pregnancy has been determined; this has been the most popular method. 2. The weight lost at delivery and in the puerperium has been determined. The assumption is that a woman having a normal weight gain in pregnancy will return nearly to her prepregnancy weight (as will many patients with abnormal degrees of edema). 3. The "reproductive weight" has been estimated by adding together the weights of the conception product, and the increase in weight of the hypertrophied uterus and adnexa, and of the breasts. To this, later authors have added factors for the increased blood volume, and made varying estimates for physiologic edema, nitrogen storage, and other "necessary" changes. 4. A few studies of weight gain have been made in other pregnant animals.

In general, the first method gives the highest average. The second and third methods have checked somewhat better at about 5 pounds less than by the first. Different estimates and guesses as to the magnitude of changes in the maternal organism, not all of which are appreciated, introduce a considerable variation in the third approach. The few studies in other animals show a net gain to the maternal tissues, but it is uncertain whether a strictly proportionate change can be assumed for the human organism. The third and fourth methods will not be discussed except incidentally in the section on what constitutes the weight gain in pregnancy.

Weight Changes During Pregnancy.—Many of the available data bearing on the weight gain in pregnancy are not strictly comparable. Some series have included toxemias while others have rigidly excluded them; some have excluded patients showing edema and others have not.

TABLE I. SUMMARY OF WEIGHT GAINS IN NORMAL PREGNANCY

| AUTHOR | YEAR | LOCALITY | CASES | WEIGHT GAIN, IN POUNDS | | | | RATE OF GAIN IN LAST TRI-MESTER POUND/WEEK | WEIGHT GAIN RELATED TO | | |
|---|------|-------------|------------|------------------------|-------------------|------------------|-------|--|------------------------|------------|----------------------|
| | | | | FIRST TRI-MESTER | SECOND TRI-MESTER | THIRD TRI-MESTER | TOTAL | | WEIGHT | AGE | PARITY |
| Gassner ²³ | 1862 | Munich | 8 to 89 | | | | | 1.03 | Heavy gain more | | Multiparas more |
| Góth ²³ | 1881 | Kolozsvár | 80 | | | | | 0.32 | Heavy gain more | | Multiparas gain more |
| Baum ² | 1887 | Munich | 16 | | | 13.6 | | 0.98 | Heavy—more | | Multiparas more |
| Krüger ¹⁰ | 1909 | Halle | 10 to 57 | | | | | 1.02 | Heavy—more | Old more | Multiparas more |
| Zangemeister ⁶³ | 1916 | Marburg | 300 | | | 12.5 | | 0.88 | Heavy—more | | No |
| Lorenzen ¹¹ | 1922 | Jena | 78 | | | | | 1.06 | Heavy—more | Young more | Multiparas more |
| Davis ¹⁵ | 1923 | Milwaukee | 150 | | | | 21.0 | | | | |
| Kemper ³⁴ | 1924 | Marburg | 22 to 345 | | 6.8 | 9.4 | | 0.71 | Heavy—more | Young more | Multiparas more |
| Hannah ²⁵ | 1925 | Dallas | 236 | | | | 13.3 | | | | |
| Randall ⁵⁶ | 1925 | Rochester | 300 | 3.5 | 7.9 | 11.1 | 22.5 | 0.85 | | | Primiparas more |
| Kerwin ³⁷ | 1926 | St. Louis | 127 to 260 | | 10.1 | 6.4 | | 0.47 | | | Primiparas more |
| Slemmons and Fagan ⁶⁰ | 1927 | Los Angeles | 500 | | | | 16.5 | | | | |
| Trillat ⁶² | 1928 | Lyon | 252 | | | 11.0 | 21.1 | 0.82 | No | | Multiparas more |
| Plass and Yeakam ⁵² | 1929 | Iowa City | 48 | | | | 37.4 | | | | |
| Rowe, Gullivan and Matthews ⁵⁷ | 1931 | Boston | 77 | | | 13.4 | | 1.01 | | | |

*Gains for the last 6 months of pregnancy.

P = Primiparas.

M = Multiparas.

| | | | | | | | | | | | | |
|------------------------------------|------|------------------|-------|-----|-----------------|-----------------|-----------------|--------------------------------------|-----------------|------------|-----------------|-----------------|
| Bingham ⁷ | 1932 | East Orange | 1,288 | 2.9 | 10.0 | 7.0 | 19.9 | 0.53 | No | Young more | No | Primiparas more |
| Siddall and Mack ⁵⁸ | 1933 | Detroit | 624 | | | 12.8 | 22.0* | 0.96 | | | | |
| Hanley ²⁷ | 1934 | Los Angeles | 482 | | | | 24.5 | 0.79 | | | | |
| Lawson ⁴² | 1934 | Washington | 220 | 0.0 | 14.0 | 10.5 | 24.1 | 0.79 | | | No | |
| Cummings ¹³ | 1934 | Ann Arbor | 937 | 0.5 | 13.1 | 10.5 | | 1.25(?) | | | | |
| Harding and Van Wyck ²⁹ | 1934 | Toronto | 719 | | | | | | | | | |
| Wodon ⁶⁵ | 1935 | Brussels | 311 | | | | 20.0% | | Heavy gain more | | | |
| Frýza ²¹ | 1937 | Ostravě | 344 | | | | | 0.95 | | | No | |
| Evans ²⁰ | 1937 | Cornwall | 159 | | | 8.4 | | 0.63 | | | No | |
| Mellroy and Rodway ⁴⁶ | 1937 | London | 1,000 | | | 9.9 | | 0.74 | Light—more | Young more | No | |
| Pugliatti ⁵⁵ | 1937 | Milan | 200 | | | | 22.0 | | Heavy—more | Young more | No | Multiparas more |
| Brays | 1938 | Duluth | 69 | | | | 23.7 | 0.77 ^P | No | No | No | Multiparas more |
| Cova ¹² | 1938 | Turin | ? | | | | | 1.08 ^M | | Young more | | |
| Mauks ⁴⁸ | 1939 | Budapest | 208 | | | 9.2 | 22.0 | 0.70 | | | No | Multiparas more |
| Bertini ⁵ | 1939 | Turin | 228 | | | | 24.6* | 1.10 ^P | | | | |
| Standar and Pastores ⁶¹ | 1940 | New York | 2,502 | 2.7 | (11.4%) 14.6 | (10.5%) 13.4 | (24.1%) 30.7 | 0.73 ^M (0.75%) 0.96 | Heavy—more | | No | |
| Granger ²⁴ | 1941 | Rockville Center | 100 | | | | 23.3 | | | | | |
| Beardsley ³ | 1941 | Engene | 200 | 0.8 | 12.4 | 11.6 | 24.8 | 0.87 | Light—more | | Primiparas more | |
| Kuo ⁴¹ | 1941 | Peiping | 200 | 1.0 | 12.3 | 10.0 | 23.3 | 0.75 | Light—more | Young more | Primiparas more | |
| Dieckmann ¹⁶ | 1941 | Chicago | ? | | | | 24.0 | 0.99 | | | | |
| Waters ⁶³ | 1942 | Jersey City | 3,230 | 3.2 | 8.0 | 12.0 | 23.2 | 0.92 | Light—more | Young more | | |
| Kerr ³⁶ | 1943 | Boston | 500 | | | | 22.9 | | | | | |
| Chesley and Chesley ¹¹ | 1943 | Jersey City | 1,180 | | | | 23.5 | | | | | |
| Averages | | | | 2.5 | 10.8 | 11.2 | 24.0 | 0.86 | | | | |
| Average of individual averages | | | | 1.8 | 10.9 | 10.7 | 23.1 | 0.82 | | | | |

In some series no dietary control or recommendations have been made, and in others vigorous efforts have been made to hold down the weight gain by restriction of calories, or of salt, or of both.

Table I summarizes some aspects of the literature. All data are given in pounds rather than kilograms since most physicians use the avoirdupois system. Since various authors have approached the problem in different ways, and with different purposes, some violence has occasionally been done in fitting their data to the Procrustean bed which such a summarizing table must be. Thus, for instance, in determining the average weight gain in the last trimester, extrapolations have been made from 12 weeks, and interpolations from 16 weeks. In these calculations, a trimester has been taken as 13.3 weeks. Whenever possible, the gain for the last trimester was computed from the data in Table II. In some of the earlier papers, more than one answer can be derived, because of the varying numbers of patients weighed at different times.

The *average* total gain in normal pregnancy, calculated from the patients' statements as to their prepregnancy weights, is 24.0 pounds (19 publications with 11,960 cases, Table I). The average of the averages is 23.1 pounds, and the range of averages is from 13.3 pounds²⁸ to 37.4 pounds.⁵² Fourteen of the 19 averages fall between 20 and 25 pounds.

The *range* of weight gains to be expected in normal patients is harder to derive, since no publication gives a standard deviation (σ) or a similar statistical factor for variability. The papers of Bingham,⁷ of Waters,⁶³ and of Chesley and Chesley¹¹ do give the numbers of patients in different weight gain categories, thus permitting the calculation of their standard deviations. These papers are based on large series, totaling half of all reported cases of Table I although Waters unfortunately includes toxemia cases. The standard deviations, as percentages of the respective means (*i.e.*, coefficients of variation) are 45.5, 45.3, and 45.8 for these 3 series. It would, then, seem permissible to assume for the pooled data of Table I, a standard deviation equal at least to 45 per cent of the grand average gain of 24.0 pounds; *i.e.*, $\sigma = 10.8$ pounds.

In a normal frequency curve, the mean $\pm \sigma$ includes 68.26 per cent of all cases, while the mean $\pm 2 \sigma$ includes 95.46 per cent of the total. Although the curve derived from Waters' data is slightly skewed, this relation holds within less than 1 per cent.

Applying these relations to the pooled data of Table I, it would appear that about $\frac{2}{3}$ of *normal* patients may be expected to gain between 13 and 35 pounds. Half of the remaining cases, or about $\frac{1}{6}$ of all, may be expected to gain more than 35 pounds. Such gains may horrify the clinician who tries to hold the weight gain below 20, or even below 15 pounds, but in a certain proportion of patients they are normal. Perhaps one might differentiate between weight gain in normal pregnancy and normal or desirable weight gain in pregnancy. This may well be a valid differentiation, since there is evidence that the greater gains are associated with an increasing incidence of certain complications.

Weight Changes in Each Trimester.—It is generally agreed that, on the average, the weight drop which may occur during the phase of anorexia and vomiting and in some patients is just about compensated in the last weeks of the first trimester and by other patients. Thus the net weight change is usually slight—perhaps an average gain of 1 to 3 pounds.^{7, 12, 41, 42, 52, 56, 61-63} From the 8 papers (8,877 cases) giving the necessary data, the average gain (weighted by numbers of cases) is 2.5 pounds for the first trimester.

By the end of the first trimester, a fairly steady rate of weight gain begins. One might expect that the rate of gain would be greater in the third trimester, since the absolute growth of the conception product is greatest at this time. Actually the published data are not all in agreement with this expectation, or with each other. In 7 of the 10 relevant papers, the greater gain is found in the second trimester (averages of 5,474 cases). In 3 papers (3,864 cases), the greater average gain is found in the last trimester. The average difference is 0.91 pounds in favor of the second trimester. None of the differences is very marked, being less than 3 pounds in 6 of the 10 papers. The greatest difference⁶³ is 4 pounds, in favor of the last trimester.

When all of the cases in Table I are pooled, the average gain in the last trimester comes out as 11.2 pounds (18 papers with 12,026 cases), while that for the second trimester is 10.8 pounds (10 papers with 9,338 cases).

One factor which perhaps makes for a greater gain in the second trimester, in some patients, is the replacement of weight lost during the anorexia and vomiting of early pregnancy. However, this is usually compensated in the averages (see above), although in some series it may not have been. Another factor, tending to reduce the average gain in the last trimester, is the prelabor weight loss. Some authors have taken account of this by weighing the patient in early labor. Other authors have computed their weight gains from the weight at the last antepartum visit, which often does not take account of this loss—when it occurs (see below).

Terminal (Prelabor) Weight Loss.—Zangemeister⁶⁶ reported that 98 per cent of his patients reached their maximal weight some time before the onset of labor—most commonly on the third day ante partum. There was then a weight loss averaging 2.2 pounds.

This finding has been confirmed,^{35, 47, 50} and denied. Kemper³⁵ gives an excellent discussion of sources of error in determining this weight loss. Many of the published reports do not conform to the criteria laid down by Kemper. In such papers, many of the weight losses are missed. Some (German papers) do meet Kemper's specifications and yet disagree with Zangemeister. When an average weight curve is drawn, it frequently shows the prelabor weight loss (see, for example, Stander and Pastore⁶¹). Individual cases are much more variable, and often fail to show the terminal weight drop. Of 15 papers, other than the five mentioned, the weight loss was noted in only from 17 to 40 per cent of 4,026 cases,^{4, 5, 13, 14, 20-22, 33, 44, 46, 51, 58} and in 63 to 75 per cent of cases.^{6, 41, 48} Krüger,⁴⁰ and Stander and Pastore⁶¹ remark on its occurrence, but do not give the frequency. The range of the average losses reported is from 0.5 to 2.4 pounds. A few of these papers are included in Table II.

In summary, it would appear that the average weight gains by trimesters are about 2.5, 10.8, and 11.2 pounds, adding up to 24.5 pounds. The average total gain, from Table I, is 24.0 pounds. (The discrepancy is caused by different papers being averaged to get the gains for different periods). The standard deviation is so great that only $\frac{2}{3}$ (if that many) of normal patients may be expected to gain 24.0 ± 10.8 pounds. The other $\frac{1}{3}$ will show weight changes departing even more radically from the average. A large proportion of patients have a terminal weight loss, but its appearance seems to be inconstant.

The Rate of Weight Gain in the Last Trimester.—The rate of gain toward the end of pregnancy is probably of more significance than is

the total gain for the whole period of gestation, when we come to consider the detection of incipient pre-eclampsia. There are 2 reasons for this: (1) In the great majority of cases, pre-eclampsia appears in the last trimester, and (2) *rapid* weight gains, especially at this time, have usually been interpreted as meaning water retention (edema formation) which is often a harbinger of pre-eclampsia. It is, therefore, important to determine the range and average of normal rates of gain at this time. Some data are given in terms of pounds per week, and some as pounds per month, which may be confusing if not carefully read.

From Table I, the average rate of gain in the last third of pregnancy is 0.86 pounds per week (24 papers with 13,500 cases). The average rates given by 25 different authors range from 0.47 to 1.25 pounds per week, with 64 per cent of the averages falling between 0.7 and 1.0 pounds per week. The average of the averages is 0.82 pounds per week. In many cases, these average rates of weight gain are derived by extrapolation or interpolation from data given for 8 or 12 weeks, or for 16 weeks. However, it would seem that the rate of gain is not constant over this whole period, and slight errors are introduced by the calculations.

TABLE II. THE DECREASING AVERAGE GAIN BY LUNAR MONTHS, AS NORMAL PREGNANCY APPROACHES TERM

| AUTHOR | CASES | WEIGHT GAINED, POUNDS LUNAR MONTH | | | | AP WEIGHT LOSS |
|-----------------------------------|-----------|--------------------------------------|-----|-----|---------|-------------------|
| | | 7 | 8 | 9 | 10 | |
| Gassner ²² | 8 to 89 | - | 5.3 | 3.7 | 3.4 | - |
| Krüger ⁴⁰ | 10 to 57 | 3.6 | 3.6 | 4.6 | 4.2 | In many |
| Zangemeister ⁶⁶ | 300+ | - | 3.4 | 3.4 | 4.0 | In 98% |
| | | | | | (0.4)† | |
| Lorenzen ⁴⁴ | 78 | - | - | 3.0 | 3.7 | In 17.1% |
| Kemper ³⁴ | 22 to 300 | 2.4 | 2.4 | 3.1 | 3.1 | In 77% |
| Trillat ^{62*} | 65 to 268 | 3.4 | 3.8 | 3.3 | 2.7 | - |
| Siddall and Mack ⁵⁸ | 624 | 4.4 | 3.9 | 4.1 | 3.3 | In 24% |
| Lawson ^{42†} | 220 | 5.0 | 4.8 | 2.8 | 0.2 | - |
| McIlroy and Rodway ⁴⁶ | 1,000 | 3.4 | 3.1 | 2.9 | 2.6 | In 22% |
| Frýza ²¹ | 344 | 3.3 | 3.3 | 3.3 | 3.8 | In 32% |
| Kuo ^{41*} | 200 | 3.4 | 3.4 | 3.1 | 2.6 | In 75% |
| Stander and Pastore ⁶¹ | 2,502 | 4.6 | 4.0 | 4.1 | 2.3 | Yes |
| | | | | | (-0.1)‡ | |
| Average | | 4.2 | 3.7 | 3.6 | 2.6 | |

*Interpolated from data for calendar months.

†From graphs.

‡Taking account of prelabor loss.

Table II shows a breakdown of the weight gains by lunar months. Seven of the 12 papers represented therein show the least gain in the last month; the other papers, with the exception of Zangemeister's,⁶⁶ Kemper's³⁴ and Frýza's²¹ either do not give data for time periods before the ninth lunar month, or are based on very few observations before that time. The data of Zangemeister and of Kemper, for the tenth month, do not include the prelabor weight loss. When this is considered, the net weight gain becomes least in the tenth month. Frýza's paper was available to me only in abstract, and I do not know whether the gain was computed from the maximal weight or from the final weight. The averages of each column in Table II show a progressive slowing in the rate of gain in the last 4 lunar months. This is particularly interesting since the absolute growth of the conception product is increasingly great during this period.

There are not many quantitative data available as to the variability of rates of gain in late normal pregnancy. Gassner²² found weight changes varying from 0 to 13.2 pounds in the tenth lunar month (average 3.39 pounds). The standard deviation calculated from his data is 99 per cent of the mean! This signifies that about 34 per cent of the patients gained between average and up to twice the average, while 16 per cent gained even more. Lorenzen⁴⁴ remarked that the rate of gain in the last 2 lunar months varied markedly from patient to patient, and in many patients it fluctuated widely from time to time. Trillat⁶² found an average rate of gain of 0.82 pounds per week, with a range from minus 0.7 to plus 3.5, in the last trimester of normal pregnancy. Rowe and associates⁵⁷ found an average gain of 1.01 pounds per week, with a range from 0 to 2.27 pounds. Harding and Van Wyck²⁹ considered as normal any gain up to 5 pounds per calendar month (their average?). Gains of more than 8 pounds per month were found in 7.7 per cent of their normal patients. Evans²⁰ reported an average gain of 2.8 pounds per (calendar?) month, with 33 per cent of normal cases gaining more than 5 pounds, and 21 per cent gaining more than 6 pounds per month in some month (s). The average of *maximal* gains per month, in any of the last 3 or 4 months, was 4.5 pounds. For Dieckmann's 140 normal patients (private communication) the standard deviation is 40 per cent of the mean weekly gain.

Frequency distributions of periodic weight gains in the last 16 weeks of pregnancy are provided in the excellent paper of Siddall and Mack,⁵⁸ and also by McIlroy and Rodway.⁴⁶ While these data indicate the range of variation in each period (*e.g.*, 24 to 28 weeks, or 32 to 34 weeks, etc.), they are of only limited value because they unfortunately do not show the total number of patients deviating from average of *any* period toward the end of pregnancy. Table III has been derived by recalculation

TABLE III. THE INCREASING VARIABILITY IN RATE OF WEIGHT GAIN AS NORMAL PREGNANCY APPROACHES TERM

Percentages refer to proportions of patients showing weight gains of at least twice average normal for the given period

| AUTHOR | CASES | 24 TO 28 WEEKS | 28 TO 32 WEEKS | 32 TO 34 WEEKS | 34 TO 36 WEEKS | 36 TO 38 WEEKS | 38 TO 40 WEEKS | PROPORTION OF PATIENTS SHOWING GAINS OF AT LEAST TWICE AVERAGE, IN AT LEAST ONE PERIOD |
|-------------------------------------|-------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---|
| Siddall and Mack ⁵⁸ | 460 | 4.6% | 6.1% | 11.2% | 14.6% | 17.5% | 35.2% | 45.0% |
| McIlroy and Rodway ⁴⁶ | 1,000 | 7.3% | 8.1% | 12.8% | 12.2% | 20.8% | 28.1% | ? |

of the data in these 2 papers. It will be seen that the rate of gain shows a striking increase in variability as pregnancy approaches term. In Siddall's and Mack's series, 45 per cent of the patients showed at some time a gain of at least twice the average for the period in which it occurred. A comparable datum is not provided by McIlroy and Rodway. (Incidentally, let the reader beware in accepting the general averages in this latter paper. The 704 primiparas and 296 multiparas were analyzed separately, and to obtain the averages for all cases the authors apparently added together the 2 averages and divided by 2. This, of course, does not give the arithmetic mean for all cases.)

In summary, the rate of weight gain in the last trimester is markedly variable, and the variability increases as pregnancy approaches term.

Factors Affecting Weight Gain During Pregnancy.—The factors which will be considered are summarized in Table I.

1. *Initial Body Weight.*—In 9 papers (3,898 cases) it was found that heavier women gain more on the average, than the lighter ones. Four papers, with 4,630 cases, came to the opposite conclusion,⁴ while in 3 papers (945 cases) it is stated that there is no significant difference. Gassner²² concluded that the gain was roughly in proportion to the initial body weight, and this conclusion was accepted by the subsequent workers in Germany. Wodon⁶⁵ carried the concept further in setting the normal average gain at 20 per cent of the initial weight, which figure was also accepted by Pugliatti.⁵⁵ Stander and Pastore⁶¹ set the normal average gain at 24.1 per cent of the weight at 6 weeks (essentially equal to the initial weight). For an already overweight woman, this seems to be rather extravagant. Not many obstetricians would accept with equanimity gains averaging 50 pounds in their 200-pound patients. (This is not to deny the tendency to such gains.)

2. *Age.*⁴—In 8 papers (5,885 cases)¹ it is concluded that young women gain more than old. Only 1 paper (Krüger,⁴⁰ 57 patients) comes to the opposite conclusion, that the older patients gain more. Bray⁸ (69 cases) found no difference in the 3 age groups into which he divided his cases.

3. *Parity.*¹—Twenty-one papers⁴ reach a conclusion as to the relation between parity and weight gain. In 8, with 5,799 cases, it is stated that there is no significant difference between primiparas and multiparas.¹ Another 8 papers (1,249 cases) find a greater gain in multiparas, while 5 papers (1,418 cases) report a greater gain in primiparas. Where differences are found, they usually are not very great, and are probably not truly significant. This is well shown in the paper of McIlroy and Rodway; the multiparas had a somewhat greater average weight gain, but when the frequency distribution curves are plotted for different weight gain classes, one can see at a glance that the primiparas and multiparas do not differ.⁴

Twin Pregnancy.—Except for a few scattered cases, the only available data on the weight gain in normal twin pregnancy are supplied by Stander and Pastore.⁶¹ In 95 normal cases, they found an average gain of less than in single pregnancy, *i.e.*, 21.1 per cent of the weight at 6 weeks as compared with the 24.1 per cent gain in single pregnancy. .

Weight Changes at Delivery and in the Puerperium (Normal Cases)

The weight changes occurring in normal patients at delivery and in the puerperium are summarized in Table IV. Gassner's²² series included some edematous patients, and for that reason his data for puerperal weight loss are higher than would be the case for strictly normal subjects. Leaving his figures out of consideration for the moment, the average total weights lost from just ante partum to about the tenth day post partum are in fairly good agreement as among the 12 published papers. The average weight loss for all patients (roughly 4,000) is 17.9 pounds, with a range of published averages running from 15.1 to 21.7 pounds (Gassner's average: 25.5 pounds). The average of the averages is 18.7 pounds (or omitting Gassner's, 18.1 pounds).⁴

The data of Table IV cover only the first 6 to 14 days of the puerperium. There are not many data available which bear on the weight changes occurring in the later puerperium. Gassner weighed 10 of his patients at 3 to 6 weeks after delivery, and found that all had gained weight since discharge from the hospital. However, in his day, the management of the puerperium involved a low caloric intake, which, together with the inclusion of edematous patients, perhaps contributes to his large weight losses (av. 10.1 pounds) of the first week after delivery. Stander and Pastore⁶¹ weighed an unspecified proportion of their 2,502 normal patients at 6 weeks post partum, and found an average loss of 1.5 pounds occurring between the tenth day and sixth week after delivery. The average weight at the sixth week post partum was somewhat greater than the average prepregnancy weight; for primiparas the difference was 4.8 pounds, and for multiparas 3.7 pounds. (Because of the different numbers of patients weighed at various times, the figures do not "add up." The gain to maximal weight averaged 30.7 pounds. The losses were: prelabor 2.42, delivery 11.75, early puerperal 5.06, and late puerperal 1.50 pounds. These losses total 20.7 pounds, or 10 pounds less than the weight gained during pregnancy, leaving 5 to 6 pounds unaccounted for in the averages.) Waters⁶³ gives no detailed data, but states that "Roughly, in the latter group (tissue gainers as differentiated from water gainers, L. C. C.) it may be said that patients will retain beyond six weeks 60 to 80 per cent of all weight gained in excess of 22 pounds," and "postpartum weight loss is within 5 pounds of the total gain for all patients who gained the average poundage."

There is not much which can be said about the variability of the weight lost at delivery and in the early puerperium, because very few relevant data have been published. Apparently, however, this weight loss varies within a considerably narrower range than does the gain during pregnancy. For instance, the standard deviation, calculated from Gassner's data on weight loss, is only 24.2 per cent of the mean. This may be compared with σ for his data on weight change in the tenth month ($\sigma = 99$ per cent of the mean). Gassner's antepartum gains, and puerperal losses probably vary more than would be found in strictly normal patients, since he included some edematous cases. The standard deviations for Baumm's² data on weight losses at delivery and in the following 6 days are 15.4 and 34.6 per cent of the respective means.

The delivery plus early puerperal weight losses in normal twin pregnancy are considerably greater than can be accounted for by adding the weight of the second child to the losses sustained after single pregnancy. The average loss is 26.8 pounds for the 172 cases in Table IV (excluding Baumm's² obviously abnormal case, and those of Mauks⁴⁸ whose number is uncertain). Stander and Pastore⁶¹ found that, as compared with single pregnancy, twin pregnancy showed a lesser gain antepartum, and a greater loss both at delivery and in the early puerperium. In the last 5 weeks of the puerperium, there was a gain in weight as contrasted with the further loss sustained by women having single pregnancies.

In summary, the delivery plus puerperal weight losses average about 18 pounds. Many patients fail to return to their pre-pregnancy weights, and the greater the gain during pregnancy (excluding water-gainers), the greater is the net gain left to the maternal organism. This constitutes a good reason for limiting the weight gain in pregnancy to about 20 pounds, as many a husband who married a slip of a girl could testify.

TABLE IV. THE AVERAGE WEIGHT LOSSES SUSTAINED AT DELIVERY AND IN THE EARLY PUERPERIUM: NONTONIC CASES

| AUTHOR | YEAR | LOCALITY | CASES | SINGLE PREGNANCY | | | TWIN PREGNANCY | | | |
|---|------|-------------|------------|-------------------------|---------------------------------|--|----------------|-------------------------|---------------------------------|--|
| | | | | POUNDS LOST AT DELIVERY | POUNDS LOST IN EARLY PUERPERIUM | DELIVERY PLUS EARLY PUERPERAL LOSSES, POUNDS | CASES | POUNDS LOST AT DELIVERY | POUNDS LOST IN EARLY PUERPERIUM | DELIVERY PLUS EARLY PUERPERAL LOSSES, POUNDS |
| Gassner ²² | 1862 | Munich | 189 to 282 | 14.44 | 10.06 | 25.5 | 2 | 26.00 | 12.37 | 38.4 |
| Kleinwächter ³⁸ | 1874 | Prague | 6 | | 6.19 | | | | | |
| Klemmer ³⁹ | 1876 | Dresden | 24 | | 1.70 | | | | | |
| Solovjev ^{40a} | 1879 | Kazan | 40 | 16.5 | 1.70 | 18.2 | | | | |
| Góth ²³ | 1881 | Kolozsvár | 10+80 | 14.5 | 7.70 | | | | | |
| Baum ² | 1887 | Munich | 60 | 13.73 | 8.01 | 21.7 | 1 | 23.22 | 28.85 | 52.1 |
| Heisl ³¹ | 1896 | Heidelberg | 100 | | 5.06 | | 1 | | 17.43 | |
| Krüger ⁴⁰ | 1909 | Halle | 49 | | | 18.6 | | | | |
| Zangemeister ²⁰ | 1916 | Marburg | 77 | 13.05 | 3.54 | 16.6 | | | | |
| Kemper ³⁴ | 1924 | Marburg | 339 | 12.32 | 2.76 | 15.1 | 11 | 20.95 | 4.11 | 25.1 |
| Kerwin ³⁷ | 1926 | St. Louis | 152 | | | 16.3 | | | | |
| Plass and Yoakam ⁵² | 1929 | Iowa City | 48 | | | 19.8 | | | | |
| Rowe, Gallivan and Matthews ⁵⁷ | 1931 | Boston | 77 | | | 19.6 | | | | |
| McIlroy and Rodway ⁴⁶ | 1937 | London | 710 | | | 20.5* | | | | |
| Brays | 1938 | Duluth | 64 | | 6.24 | | | | | |
| Mauks ¹⁸ | 1939 | Budapest | 208 | | | 17.6 | 9 | | | 26.2 |
| Guttmacher ²⁵ | 1939 | Baltimore | | | | | 64 | | | 26.2 |
| Bertini ⁵ | 1939 | Turin | 64 | | | 19.3 | | | | |
| Stander and Pastore ⁶¹ | 1940 | New York | † | 11.75 | 5.06 | 16.8 | 95 | 17.45 | 9.75 | 27.2 |
| Chesley and Boog ⁷⁰ | 1943 | Jersey City | 16 to 30 | 10.28 | 5.46 | 15.8 | | | | |
| Averages | | | | 12.0 | 5.2 | 17.9 | | 18.0 | 9.5 | 26.8 |
| Average of averages | | | | 12.6 | 5.4 | 18.7 | | 21.9 | 14.5 | 32.5 |

*Weight lost from just ante partum to 6 weeks post partum.

†Unspecified proportion of 2,502 patients. In calculating the averages, 2,400 were assumed for the delivery losses, and 2,000 for the early puerperal losses.

Relation of Weight Gain to Toxemia

Insofar as possible, "toxemia" will refer to pre-eclampsia and eclampsia, as defined by the American Committee on Maternal Welfare. Unfortunately, some of the papers do not differentiate between the different classes of toxemias.

Gassner,²² in 1862, correlated excessive puerperal weight losses with diuresis and the discharge of edema fluid which had been accumulated during pregnancy. However, Zangemeister⁶⁶ in 1916, was the first to emphasize that edema formation and incipient toxemia could be detected by periodic weighings of pregnant women.

Some writers have not made a distinction between water gain and "stereoplastic gain" (Waters' term), and have regarded any excessive weight increase as a harbinger of toxemia. Indeed, it has been conceived that overloading the maternal organism with stored fat and protein may of itself lead to toxemia. However, the consensus of opinion today is that weight gains significant for the development of toxemia represent water retention. While weight taking is obviously nonspecific, it is of some value in that rapid and excessive gains in weight have been interpreted as pointing to water accumulation. As mentioned before, the rate of gain in the last trimester is probably of more significance than is the total gain in pregnancy.

Total Weight Change in Toxemia.—Table V shows 7 publications in which the average total weight gains are compared for normal and for toxic pregnancies. Randall,⁵⁶ with only 12 cases of toxemia, found the average normal weight gain to be doubled in the toxemia patients. At the other extreme, Stander and Pastore⁶¹ report that the average total weight gain in their 2,502 normal patients was essentially the same as in their 177 cases of mild and severe pre-eclampsia (mild pre-eclampsia taken as the equivalent of their "low reserve kidney"). In their 30 cases of eclampsia, the average gain was slightly greater (being about 2.5 pounds above average normal), but most of the extra gain occurred in the last week or two. Their data for total gains, in percentages of the weight at 6 weeks, are: normals 24.1, "low reserve kidney" 24.46, pre-eclampsia (severe, L. C. C.) 25.15, and eclampsia 26.15. In the other 5 publications, the average total gain in toxemic patients ranges from 2 to more than 6 pounds above the respective averages for normal patients. If one were able to plot frequency distribution curves for total weight gains in normal and in toxemic patients, it would seem that most of the toxemic patients would fall within the normal range, and nearly half would have less than average "normal" gains.

Another approach to the question is summarized in Table VI. As the total weight gain becomes greater, the incidence of toxemia increases. Bingham⁷ and Chesley and Chesley¹¹ are the only authors to give data for the numbers of normal and of toxemic patients in each weight gain category, and they did find that the incidence of toxemia mounted as the weight gain increased. However, 72 per cent of the toxemia cases in each series had weight gains of less than 30 pounds. About 88 per cent of the patients, in each series, who gained more than 30 pounds did not have toxemia.

Dieckmann and Brown¹⁷ found that 57 per cent of about 570 pre-eclamptics gained less than 22 pounds, and 71 per cent less than 26.5 pounds.

TABLE V. COMPARISON OF NORMAL AND TOXIC PREGNANCIES IN RESPECT TO TOTAL WEIGHT GAIN AND RATE OF GAIN IN LAST TRIMESTER

| AUTHOR | NORMAL PREGNANCY | | TOXIC PREGNANCY | | INCIDENCE OF TOXEMIA PER CENT | | INCIDENCE RATIO NORMAL GAIN ABNORMAL GAIN | ABNORMAL GAIN BEFORE OTHER SIGNS OF TOXEMIA | CASES | |
|-------------------------------------|--------------------|---|--------------------|---|-------------------------------|-------------------------|---|---|--------|---------|
| | TOTAL GAIN POUNDS | POUNDS/ WEEK IN LAST TRIMESTER | TOTAL GAIN POUNDS | POUNDS/ WEEK IN LAST TRIMESTER | IN NORMAL WEIGHT GAIN | IN ABNORMAL WEIGHT GAIN | | | NORMAL | TOXEMIA |
| | | | | | | | | | | |
| Randall ⁵⁶ | 22.5 | 0.85 | 44.5 | 3.18 | 1.3 | 6.4 | 1:5 | Yes | 300 | 12 |
| Bingham ⁷ | 19.9 | 0.53 | 25.6 | | | 5.9 | 1:1 | Yes | 1,288 | 50 |
| Siddal and Mack ⁵⁹ | | 0.96 | | 1.06 | | | (about) | In 37 per cent | 624 | 100 |
| Cummings ¹³ | 24.1 | 0.79 | >30.0 | | | 48.0 | | Yes | 937 | 63 |
| Harding and Van Wyeke ²⁹ | | 1.25 | | | 0.0 | | | Yes | 719 | 7 |
| Wodones | | 1.10* | | >1.10 | 7.9 | 76.6 | 1:10 | Yes | 311 | 89 |
| Evans ²⁹ | | 0.63 | | 1.10 | 0.6 | 49.0 | 1:82 | In 65 per cent | 159 | 52 |
| Mellroy and Rodway ⁴⁰ | | 0.74 | | 1.06 | | | | Yes | 1,000 | 75 |
| Pugliatti ⁵³ | 22.0 | ? | | Doubled | | | | Yes | 200 | 9 |
| Mauck ¹⁸ | 22.0 | 0.70 | 27.1 | 1.00 | | 30.0 | | Yes | 208 | 168 |
| Bertini ⁵ | 21.84 ^P | 1.08 ^P | 26.34 ^P | | | | | Yes | 228 | 14 |
| | 27.74 ^M | 0.73 ^M | 36.74 ^M | | | | | | | |
| Stander and Pastore ⁶¹ | 24.1 ^C | 0.75 ^C | 24.8 ^C | 0.84 ^C | | | | | 2,502 | 207 |
| Chesley and Chesley ¹¹ | 23.5 | | 25.7 | | | | | | 1,180 | 98 |

*Upper normal.

†Gain in last 6 months. White Bertini's multiparas had a greater 6-month gain than his primiparas, the latter gained faster in the last trimester.

P = Primiparas; M = multiparas.

TABLE VI. THE INCREASING INCIDENCE OF TOXEMIA CORRELATED WITH HIGHER TOTAL WEIGHT GAINS

| AUTHOR | CASES | TOTAL WEIGHT GAIN IN POUNDS | | | | | | |
|--------------------------------------|-------|-----------------------------|-------------|-------------|-------------|---------------|-------------|-----|
| | | 0 TO 10 | 11 TO 20 | 21 TO 25 | 26 TO 30 | 31 TO 35 | 36 TO 40 | 41+ |
| Bingham ⁷ | 1,338 | 0.7% | 1.5% | 5.3% | | 10.6% | | |
| Cummings ¹³ | 1,000 | | | 3.5 5.5 | | 48.0%* | | |
| Waters ⁶³ | 1,459 | | | | | 11.8 | | |
| Chesley and Chesley ¹¹ | 1,278 | 6.2% | 9.3% | 9.8% | | 12.8% 13.0% | | |

*"Showed signs of toxemia or actually developed it." Only 22 patients of the 1,000 had "large amounts of albumin"; all of these had gained more than 30 pounds. These 22 patients represent 16.8 per cent of the 131 having such gains.

• Briefly, the total weight gain in pregnancy does not seem to be of much value in detecting incipient toxemia. Many, perhaps most patients who develop toxemia have had normal total weight gains. Relatively few patients with higher weight gains do become toxemic.

Rate of Gain in Last Trimester.—All of the 8 relevant papers represented in Table V agree that toxemic patients show an augmented rate of weight gain in the last trimester. The differences between average rates of gain in normal and in toxemic patients are often not well marked. However, this may be attributable to the fact that the average rate of gain is calculated for the whole trimester, and sudden spurts occurring in one or two weekly periods are obscured. Nearly all writers are agreed that rapid weight gain frequently precedes hypertension and other signs of toxemia, often by weeks. In other cases the rapid gain coincides with the appearance of hypertension, and sometimes it does not occur at all.

It seems well established that, on the average, pretoxic patients gain weight more rapidly than the average rate for normal patients. However, there is a serious paucity of data bearing on the questions as to what is the normal range of gain, how many patients develop toxemia without abnormally rapid gains, and how many patients have abnormal rates of gain and do not develop toxemia. Most of the conclusions have been drawn from insufficiently worked data.

Siddall and Mack⁵⁹ have made a critical analysis of their data, and concluded that "the occurrence of excessive weight gains in pregnancy would appear to be of doubtful significance in predicting impending toxemia." They found that 61 per cent of their 100 toxemia cases had weight gains of at least twice average at one or more periods after the seventh lunar month. The other 39 per cent "had no excessive gain at any time," and in the last four months gained an average of only 11.6 pounds as compared with 15.7 pounds in normal patients. Of the 61 patients who did have excessive rates of gain, the rapid gain preceded hypertension in 37 cases. "Since excessive weight increase preceded other signs in 37 per cent of toxemias, it might seem of real value in discovering the disease in its incipency." But, as was pointed out in the section on rate of gain in normal pregnancy, these workers found that 45 per cent of normal patients also showed comparably excessive gains at one or more periods in the last 4 months. "Consequently, our figures indicate that acceptance of excessive gain as reliable evidence of incipient toxemia necessities subjecting approximately one-half of all

pregnant women to treatment." Table III offers perhaps the only escape from these conclusions. As normal pregnancy approaches term, the variability of weight gain increases markedly, and in the last 2 weeks, 35.2 per cent of Siddall's and Mack's patients showed gains of at least twice the average for this period. If a large proportion of the 45 per cent showing twice average gains at any time, had the abnormal gains only in the last 2 weeks, then the gains occurring earlier in pretoxic patients would have added significance. It is hardly fair to expect excessive gain to predict future toxemia if that gain occurs when delivery is imminent. Unfortunately, one cannot determine this point from the published data.

¶ The two papers in which excessive rates of gain have been alleged to be most closely correlated with the development of toxemia are those of Wodon⁶⁵ and of Evans.³⁰ In discussing Evans' paper, Siddall and Mack⁵⁹ write "conclusions were based on the records of only 211 patients (apparently a series of consecutive cases) of whom the surprising number of 52 were classified as toxemia." Wodon's series is equally astonishing—89 toxemias in 400 patients. The toxemia incidences would be: Evans, 24.6 per cent and Wodon, 22.3 per cent. Siddall and Mack question the validity of many of the diagnoses, and it seems to me justifiably so. Accepting Evans' diagnoses, we find that the average monthly gain in the toxemias was 4.3 pounds, as compared with 2.8 pounds in normal patients. A maximal gain of 5 pounds in any month almost made a separation of normal from toxic patients. Those women who never exceeded this gain had a toxemia incidence of 0.6 per cent, and only 2 per cent of all toxemias occurred in this class. In the women gaining more than 5 pounds in any month, the toxemia incidence was 49 per cent, and 98 per cent of the toxemias were associated with such gains. Exactly $\frac{1}{3}$ of the normal patients did have maximal gains of more than 5 pounds in some month.

Wodon⁶⁵ found a toxemia incidence of 7.9 per cent among 306 patients whose weekly weight gain never exceeded 1.1 pounds. In the 94 patients who did show greater gains, the incidence of toxemia was 76.6 per cent. Omitting patients whose only toxic sign was a mild elevation in blood pressure, the incidences of toxemia would be 2.3 and 20.2 per cent in the respective groups. The ratio of toxemia incidences is roughly 1:10, either with or without the questionable cases.

Harding and Van Wyck,²⁹ in a series of 726 unselected private patients, found that all of their toxemias (excluding one case of "chronic nephritis") had shown monthly gains of 8 pounds or more. No further data are given as to the distribution of weight gains. Mauks⁴⁸ states that toxemia developed in 30 per cent of his patients who gained more than 4.4 pounds per calendar month. His average monthly gains were: in normals 3.1 pounds, in mild toxemia 3.7 pounds, and in severe toxemia 5.5 pounds. Dieckmann and Brown¹⁷ found that 74 per cent of their severe pre-eclampsies gained more than 1.3 pounds per week, and 24 per cent gained more than 2.2 pounds per week. Conversely, 76 per cent gained less than 2.2 pounds per week, and 26 per cent gained less than 1.3 pounds per week. (These are apparently average figures for the whole period of observation. Maximal figures are not given, either for normals or for toxemias.) McIlroy and Rodway⁴⁶ do not give the variations in rate of gain occurring at any time, but apparently doubled gains were 3 to 5 times more frequent in toxemias than in normals.

In summary, many pretoxic patients gain weight rapidly. The absence of such gain is no insurance against the development of pre-eclampsia, and a large number of patients who will not become toxemic will scare the physician with definitely "abnormal" rates of gain. Pooling the data of Siddall and Mack,⁵⁹ of McIlroy and Rodway,⁴⁶ and of Evans,²⁰ it would seem that about 54 per cent of toxemia patients will show, at some time, a weight gain of at least twice the average for that period. Nearly 40 per cent of normal patients will show similar gains (figures approximate).

Delivery and Early Puerperal Weight Losses (Toxemias)

Zangemeister⁶⁷ found the total weight lost from just ante partum to the tenth day post partum to average 27.1 pounds in 8 patients with "hydrops gravidarum." The average loss in his normal patients was 16.6 pounds. Bertini⁵ reports the weight loss (to the seventh day) in 8 toxemias as averaging 24.9 pounds; his normal patients lost an average of 19.3 pounds. Stander and Pastore⁶¹ give figures for about 200 toxemias, whose weight loss (to the tenth day) averaged 20.6 pounds as compared with a loss of 16.8 pounds in their normals.

Presumably this excessive loss, which occurs so rapidly after delivery, represents the discharge of edema fluid. ♀

What Constitutes the Maternal Weight Gain?

The combined data of Baumm,² Gassner,²² Kemper³⁴ and Lehn⁴³ show an average weight of baby + after birth + amniotic fluid in 958 cases amounting to an average of 11.18 pounds. This is a little less than half of the total average gain shown by the mother. In about 10 per cent of 6,046 term pregnancies^{7, 11, 41, 63} this "reproductive weight" is greater than the total weight gain shown by the mothers, some of whom actually have weight losses. In such cases, of course, there has been a net loss to the maternal organism. However, in the majority of cases there accrue to the maternal tissues considerable gains in weight; in perhaps a fifth of cases this net gain, exclusive of the conception product, exceeds 20 pounds. On the average, this net gain to the maternal organism amounts to about 10 per cent of the prepregnancy weight (Net gain = total gain of 24 pounds minus 11.2 pounds of conception product = 12.8 pounds. Average prepregnancy weight = 128 pounds, according to Stander and Pastore.⁶¹)

The few studies made with other pregnant animals, summarized in Table VII, indicate net gains to the mother amounting to an average of 11.6 per cent above the expected weight. The "expected weight" is the weight of the unbred controls which were often litter mates, or at least were animals of the same age and initial weight at the time of breeding the experimental animals. Edlefsen's¹⁹ work on guinea pigs is omitted, because he used immature animals, and his only controls were males.

There are certain necessary changes in the maternal organism incident to pregnancy. First, there is the growth of the uterus and its adnexa. According to Reynolds,¹²⁴ the uterine mass increases from about 30 to 60 grams to 1,000 to 1,400 Gm., an increase of 2.07 to 3.02 pounds, or about 2.5 pounds as an average figure. Second, there is the enlargement of the breasts which varies greatly. Evans²⁰ estimates this factor at 2 to 4 pounds.

TABLE VII. THE NET GAIN IN WEIGHT ACCRUING TO MATERNAL TISSUES DURING PREGNANCY IN ANIMALS OTHER THAN WOMAN

| AUTHOR | ANIMAL USED | NO. OF ANIMALS | PERCENTAGE GAIN ACCRUING TO MATERNAL TISSUES DURING PREGNANCY | REMARKS |
|----------------------------------|-------------|---------------------|---|---|
| Minot ⁴⁹ | Guinea pigs | 66 | 15 per cent | Rapid loss of weight in first 5 days postpartum |
| Herring ³² | Rats | 9 | No gain | |
| Hartwell ³⁰ | Rats | 6 in 40 pregnancies | 13 per cent | Initial weight assumed to be 200 Gm. |
| Hain ²⁶ | Rats | 16 | 12 to 15 per cent | |
| Abramson ¹ | Rats | 44 | 6 per cent | |
| Bruhl and Vogel ⁹ | Mice | 4 | 16 per cent | Immature mice omitted (gain more) |
| Poo, Lew and Addis ⁵⁴ | Rats | 20 | 12 per cent | Up to eighteenth day of 23-day pregnancy |
| Totals and mean | | 199 | 11.6 per cent | |

Adding these components to the weight of the conception product, we can account for about 17 pounds of the total gain shown by the pregnant woman. This leaves an average of about 7 pounds, and in many cases much more, yet to be explained.

Opinion has varied greatly as to what constitutes this additional maternal gain, and as to the proportionate parts contributed by the different factors which have been recognized. In the present review, the following will be considered: 1. Protein (nitrogen), and 2. water, with electrolytes. Fat will not be discussed for want of quantitative data. Obviously, some patients gain a great deal of fat, and others very little. Because of the many facets of the problem, complete reviews of the relevant literature will not be attempted. References will be made only to summarizing papers, or to papers most germane to the topic in hand.

1. *Protein (Nitrogen) Retention.*—Hunscher and associates¹⁰⁶ in 1933 reviewed the literature on nitrogen retention in pregnancy. From 945 daily N balances, they calculated that the average retention was 2.28 grams per day over the last 8 lunar months. This would give a total N storage of 511 grams. From the available estimates in the literature, they set the N requirements as follows: fetus 70 Gm., placenta, cord and blood 18.0 Gm., amniotic fluid 0.86 Gm., breasts 17 Gm., and uterus 38 Gm.; total about 145 Gm. This would leave 366 grams for the maternal organism (exclusive of the reproductive system). In a later paper, Hunscher and others¹⁰⁷ followed a multipara continuously during the last 145 days of pregnancy, and found that she stored 446.2 Gm. of N. It was estimated that 300 Gm. of this was in the maternal tissues outside the reproductive system. Seegars¹²⁸ found a comparable N storage in a young primipara. Thompson and Pommerenke¹²⁷ found a far lesser degree of N storage in 2 women studied at different times in pregnancy. They seem inclined to accept the results in the literature

as being more typical than their own cases. Freyberg, Reekie and Folsome⁹⁶ followed a young primipara over the last 62 days of pregnancy, and found an N retention averaging only 0.82 Gm. per day in contrast to the average of 2.28 Gm. from Hunscher's summary of the literature. Oberst and Plass¹²⁰ found N retentions in 5 young primiparas which averaged close to the figure of 2.28; retention was somewhat greater in the fifth and sixth lunar months than in later pregnancy. Coons and associates⁸² found comparable N retentions in 6 patients.

It would seem, then, that about a pound of nitrogen is retained during pregnancy. Presumably this is stored as protein, which would weigh about 6 $\frac{1}{4}$ pounds. If this protein were used in the formation of new tissue, with the usual proportion of water (as in muscle tissue for instance), the expected weight increment attributable to N storage alone would be 30 to 35 pounds. Since such weight gains are not the rule, the protein (if such be the storage form) must be packed away somewhere in concentrated form.

In looking for the site of stored protein, one thinks at once of the liver. A fairly extensive search of the literature on human liver weights has turned up just one bald statement which almost seems irrelevant in the paper in which it occurs. Bean and Baker⁷¹ write "The liver in pregnant women is considerably larger than the average of the normal liver weight." They make no other mention of pregnancy, and no figures are given for livers from pregnant women. However, there are several papers describing changes in organ weights incident to pregnancy in rats and mice. Herring³² found the liver weight to increase 27.5 per cent in pregnant rats. MacKay⁴⁵ found the increase to be 20 per cent; Abramson¹ about 13 per cent. Brühl and Vogel⁹ found the liver weight in 7 white mice to increase 39 per cent. Liesenfeld, Dahmen and Junkersdorf¹¹⁵ found only slight increases in liver weight in 2 pregnant dogs, and a decrease in their third dog. Poo, Lew and Addis,⁵⁴ in 20 rats, found that by the eighteenth day of pregnancy the liver had increased about 40 per cent in weight as compared with the controls.

Poo, Lew and Addis⁵⁴ analyzed the various organs of their rats for protein content. They found a 34 per cent increase in the total amount of protein in the liver. There was also a 25 per cent increase in the protein content of the alimentary tract. The protein increment in the carcass was only 2 to 3 per cent. Of the total protein gained, 36 per cent was in the liver and alimentary tract, 36 per cent in the uterus, and 29 per cent in the carcass. The actual concentration of protein was decreased, during pregnancy, in the liver, blood, kidney and heart. That is, stored protein apparently was associated with even more than the usual proportion of water. How far these figures are applicable to human beings is questionable. Certainly the uterine growth in rats is out of proportion to that in women.

Briefly, then, it seems that at least 6 pounds of the average maternal gain during human pregnancy can be attributed to protein storage. Of this, perhaps two-thirds is to be found outside of the reproductive system. If the protein be associated with the usual proportions of water, as it seems to be in the rat, the storage in human maternal tissues would call for unreasonable weight gains of the order of 20 pounds attributable to this factor alone.

2. *Water Retention in Normal Pregnancy.*—It is generally recognized that normal pregnancy is accompanied by some degree of water reten-

tion. Since the noncolloidal osmotic relations do not seem to be significantly disturbed in pregnancy, there must be a proportional retention of electrolytes. The clinical observations indicating that water retention does occur during pregnancy are: 1. The marked postpartum diuresis (see Crabtree⁸⁴); 2. the simultaneous rapid weight loss in the early puerperium (Table IV); and 3. the atonic and flaccid condition of the tissues after the diuresis (discharge of edema fluid). A variation on the third observation is the demonstration of a shrinkage in the circumferences of the arms, legs and neck in the first few days after delivery, occurring in 95 per cent of cases (Fink,⁹⁵ Gueissaz¹⁰⁰).

Physiologic measurements pointing to water retention are: 1. The increase in venous pressure in the legs; 2. the decrease in colloid osmotic pressure of the plasma; and 3. the positive sodium balance throughout most of pregnancy. 4. Still another factor contributing to water retention during pregnancy is the presence of huge quantities of the steroidal sex hormones, which perhaps are responsible for the sodium retention.

In determining the distribution of the retained water, a considerable quantity can be allocated to the blood itself. Dieckmann and Wegner⁵⁹ (see for review of earlier work), Thomson and associates,¹³⁹ and Albers⁶⁹ have found that the total blood volume increases markedly during pregnancy. These increases were found by the authors cited to be, at term, 20 per cent, 30 per cent and 29 per cent respectively. All found that the plasma volume increased more than the cell volume. Oberst and Plass¹²¹ have shown that the water content of both plasma and cells is increased in pregnancy. The average water gain represented in the increased blood volume might be calculated as follows. The average woman's non-pregnant weight is close to 128 pounds (Stander and Pastore⁶¹), and she gains about 24 pounds in pregnancy (Table I). The data of Thomson and associates¹³⁹ show a blood volume of 30.1 ml. per pound at 30 days or more post partum (checking closely with other measurements of blood volume in nonpregnant women), and a volume of 35.1 ml. per pound in the last month of pregnancy. The difference in total blood volumes would be about 1,490 ml., or 3.45 pounds (specific gravity of whole blood as 1.055). Oberst and Plass¹²¹ give the average water content of whole blood as 811 Gm. per kilo of blood for nonpregnant women, and 827 Gm. per kilo in late normal pregnancy. The total gain in blood water then would be about 1,300 Gm., or 2.9 pounds.

The volume of the interstitial water depends upon at least 3 major factors, viz.: 1. The effective intracapillary hydrostatic pressure which impels filtration from the vascular bed; 2. the effective colloidal osmotic (oncotic) pressure of the plasma, which limits filtration and effects reabsorption of filtered water; and 3. the rate of lymphatic drainage. Also changes in capillary permeability perhaps may be operative at times. ("Effective pressures" refer to the differentials between the intra- and extra-vascular forces). Normally, these 3 factors are nicely balanced, and the interstitial fluid volume is thereby maintained with a fair degree of constancy. If the volume is to remain constant, a disturbance in one of these factors must be compensated by adjustments in the others.

In pregnancy there is an increase in capillary pressure in the legs, and the oncotic pressure is diminished. Both of these factors make for an increase in the interstitial water volume. The extent to which lymphatic drainage undergoes a compensatory increase is unknown, at least to me.

Measurements of capillary pressure have been attempted by various techniques but most of the data are unsatisfactory. The problem has therefore been approached by determinations of venous pressure. McLennan¹¹⁶ has recently reviewed the literature, and contributed a superb study made on 255 of his own subjects. He concludes that the antecubital venous pressures are not increased in normal pregnancy, agreeing therein with 8 of the 16 earlier reports which he reviewed. The femoral venous pressure rose from 91 mm. of water in early pregnancy to a peak value, at term, of about 244 mm. of water (average of 42 patients). All 7 previous reports agreed that the femoral venous pressure was increased in pregnancy. The increased femoral pressure, of course, would be considerably augmented by the assumption of the upright position—McLennan's measurements were made with the subjects supine. Róna¹²⁵ determined the saphenous pressure in pregnancy with patients standing. The average pressure at the level of the venepuncture was 938 mm. H₂O, and ranged from 792 to 1,230. These markedly elevated femoral venous pressures must be reflected in the capillaries of the legs. Since this hydrostatic pressure approaches, or on standing exceeds, the oncotic pressure (see Table VIII), there must be an increased filtration and a diminished capillary reabsorption in the legs, thus predisposing to the accumulation of interstitial fluid. The transudation is limited, of course, by the increasing extravascular tissue pressure.¹¹³ (Even in nonpregnant individuals, prolonged standing will result in a demonstrable increase in leg volume, though not visible edema, and concentration of the blood.¹³⁸) Since the legs constitute about 37 per cent of the body weight,¹⁴¹ considerable volumes of water may be thus retained. During recumbency, some or all of this accumulated water may be mobilized and excreted, thus accounting for the observation that late in pregnancy the night urine volume approaches or exceeds the day volume.¹³⁶

As Table VIII shows, the colloidal osmotic pressure of the plasma is diminished by about 20 per cent during pregnancy. This is attributable to the characteristic drop in serum proteins, amounting to about 1 gram per 100 ml. of serum.⁸⁸ As Dieckmann⁸⁸ has pointed out, this diminution in proteins and oncotic pressure is not sufficient to account for the palpable edema of either normal or toxic pregnancy (Strauss,¹³⁰ however, has attributed the edema of toxemia to decreased oncotic pressure along with other factors). While the changes in proteins occurring in normal pregnancy are not great enough to cause edema, they may well lead to some degree of water retention which would not show up as visible edema. The statement is commonly made that the body can retain water up to 10 per cent of its weight before edema becomes evident. I have not been able to find the original work upon which this statement is based. However, Drury and Jones⁹² have shown that fluid accumulation in the legs must increase by 8 per cent before edema becomes evident. Weech, Snelling and Goettsch¹⁴³ produced edema in dogs by plasmapheresis and by protein restriction. Their results "... suggest an equilibrium between plasma proteins and the volume of fluid in the interstitial spaces. The equilibrium seems to be maintained throughout the entire range of protein variation in such a way that every slight protein decline leads to a correspondingly slight increase in interstitial fluid."

Goudsmit and Louis,⁹⁹ in a quantitative study, found that a decrease in serum proteins of 1 gram per 100 ml. will result in an increase in

TABLE VIII. ONCOTIC PRESSURE OF PLASMA OR SERUM IN PREGNANCY
 Drinker and Field, in review of literature, found an average of 367 mm. H₂O for 361 nonpregnant normals. Range of averages 286 to 431

| AUTHOR | NORMAL PREGNANCY WITHOUT EDEMA | | | | NORMAL PREGNANCY, LATE, WITH EDEMA | | | PRE-ECLAMPSIA | | | ECLAMPSIA | | |
|--------------------------------------|--------------------------------|-----|----------------|-----|------------------------------------|------------|-------|---------------|------------|------------|-----------|------|-------------|
| | EARLY PREGNANCY | | LAST TRIMESTER | | CASES | MEAN | RANGE | CASES | MEAN | RANGE | CASES | MEAN | RANGE |
| Runge and Kessler ¹² | 18 | 391 | 317 to 455 | 26 | 323 | 243 to 350 | | | | | | | |
| Kaboth ¹⁰ | | | | 14 | 316 | 253 to 362 | | 7 | 263 | 180 to 342 | 7 | 231 | 188 to 277 |
| Kýlin ¹¹ | | | | | | | | 7 | 228 | 143 to 315 | 2 | 220 | 196 and 245 |
| Baráth and von Magyary ²⁰ | | | | 3 | 317 | 314 to 322 | 4 | 318 | 311 to 328 | | | | |
| Orr ²² | 14 | 348 | 303 to 405 | 42 | 297 | 261 to 392 | 14 | 293 | 273 to 336 | | 4 | 284 | 272 to 296 |
| Martines and De Lauretis | 14 | 259 | 170 to 376 | 56† | 245 | 138 to 394 | | 2 | 236 | 230 to 243 | 5 | 284 | 212 to 346 |
| Diekmann and Kramers | | | | 15 | 287 | 226 to 381 | | 22 | 255 | 210 to 301 | | | |
| Totals and averages | 46 | 338 | 170 to 455 | 156 | 284 | 138 to 394 | 18 | 298 | 273 to 336 | | 42 | 254 | 143 to 342 |
| | | | | | | | | | | | 19 | 239 | 160 to 346 |

*Omitting 3 extremes range would be 275 to 332.

†One patient counted twice.

‡Some probably had edema.

TABLE IX. SODIUM RETENTION DURING NORMAL PREGNANCY

The last column is calculated from the assumption that all sodium is held extracellularly, is osmotically active, and that its concentration in extracellular water is 336 mg. per 100 ml.

| AUTHOR | CASES | PERIOD IN PREGNANCY | MEAN DAILY RETENTION OF Na, GM. | TOTAL RETENTION, GRAMS PER WEEK | CALCULATED GAIN IN EXTRACELLULAR H ₂ O LITERS PER WEEK |
|--|-------|-----------------------------|---------------------------------|-------------------------------------|---|
| Coons and associates ⁸¹ | 5 | Near end | 1.26 | 8.81 | 2.620 |
| Hummel and associates ¹⁰⁵ | 1 | Last 21 weeks | 0.56 | 3.92 | 1.167 |
| Freyberg and associates ⁹⁶ | 1 | Last 70 days | 0.231 | 1.61 | 0.473 |
| Thompson and Pommerenke ¹³⁷ | 1 | In fourth and eighth months | 0.44 0.267 | 3.08 1.87 | 0.917 0.557 |
| Taylor and associates ¹³² | 4 | Last 13 to 23 days | 0.440 | 3.08 | 0.917 |
| Taylor and associates ¹³³ | 3 | First 10 days p.p. | -0.489 | Total loss, first 10 days p.p. 4.89 | Total loss, first 10 days p.p. 1.455 |

interstitial water amounting to 3.8 ± 0.8 per cent of the body weight. In our average patient who has gained from an initial 128 up to 152 pounds in pregnancy, this factor would, then, account for a water gain of about 5.8 pounds.

The sodium retention of pregnancy is summarized in Table IX. In the last column of the table is shown the volume of extracellular water gain per week to be expected if all of the sodium is held extracellularly in osmotically active form, and if blood and tissue fluids are not to show any significant increase in sodium concentration (see papers of De Snoo,⁸⁶ Zangemeister,⁶⁷ Rossenbeck,¹²⁶ and of Taylor, Warner and Welsh¹³³ for review of literature, indicating that sodium concentrations are essentially unchanged in pregnancy). Since these calculated volumes of water gain are unreasonably high, some of the sodium must be stored in an osmotically inactive form. Perhaps this osmotically inactive sodium is bound to proteins, or stored in the bones. Rossenbeck¹²⁶ found from direct analysis of various tissues that the sodium content is increased in normal pregnancy, and markedly increased in eclampsia. In normal pregnancy, he calculates that the excess muscle sodium amounts to about 3 grams. This is only a fraction of the total amount stored during pregnancy.

Taylor, Warner and Welsh¹³³ provide a review of the effect of the steroidal sex hormones in sodium and water retention. "They consider that the increased venous pressure of the legs, together with the diminished oncotic pressure of the plasma, may contribute somewhat to the retention of water. "The general tendency of normal pregnant women to retain sodium and water appears, however, to be best explained by the fact that they are constantly under the influence of enormous quantities of the steroid sex hormones. This effect is so predictable from the known physiologic properties of these substances that were the tendency to sodium and water retention not present, one would have to find an explanation for its absence." An interesting observation in this connec-

tion has been made by Friedlander and associates.⁹⁷ They found that estrogen administration was followed by sharp rises in the blood volume in both human subjects and in cats. This effect, however, was found only when the blood volume was initially low. Perhaps the constant influence of enormous quantities of the steroids during pregnancy could produce a like effect upon subjects with initially normal blood volumes. A role of these hormones in premenstrual edema is suggested by Thorn and Emerson¹⁴⁰ who review some aspects of the possible relation between the sex steroids and the sodium and water retention associated with premenstrual tension and edema.

The antidiuretic substances found in the urine of many toxemic and some normal subjects will not be reviewed here. The work of Gilman and Goodman⁹⁸ suggests that if a prerenal deviation of water occurs, there might be imposed upon the kidney the necessity for water reabsorption. If this be the case, the appearance of antidiuretic substances would be secondary. For reviews of subject, see Teel and Reid,¹³⁵ Krieger and Kilvington,¹¹¹ and Ham and Landis.¹⁰¹

In summary, the blood volume increase occurring in normal pregnancy accounts for the addition of an average of 2.9 pounds of water. The diminution in serum (plasma) proteins, averaging 1 gram per 100 ml., may account for an average increase of about 5.8 pounds of water in the interstitial spaces. The increased venous pressure of the legs favors water retention at this site. This last factor tends to be self-limited because the increasing volume of interstitial fluid exerts a back pressure (tissue turgor) which offsets the intravascular hydrostatic pressure. Also, fluid accumulated in the legs while the subject is up and about is largely mobilized and excreted during recumbency. The sex steroids also contribute a quantitatively unassessed part in sodium and water retention.

There have been but very few attempts to measure the water changes occurring in pregnancy. Chesley⁷⁴ has determined the thiocyanate-available (roughly extracellular) water in a large series of cases. Measurements were made in 67 cases in early pregnancy, and repeated at about 32 to 35 weeks. In another 375 normal cases, tests were made at 31 to 33 weeks and repeated at 35 to 37 weeks; in some cases measurements were again made at term. There seemed to be a gradually increasing rate of gain in the thiocyanate-available water. The total gain in pregnancy amounted to an average of 6.3 liters (13.85 pounds), of which 1.5 to 2.0 liters were thought to be in the conception product. The rest of the water presumably represented hydration of the maternal tissues, and totaled 9 to 10 pounds. Some of this water of hydration (perhaps about 4.5 pounds) has already been counted in the weight gain components discussed above; *i.e.*, 2.9 pounds in the increased blood volume, and an estimated 1.6 pounds in the new tissue of the uterus and breasts.

Chesley and Boog⁷⁶ made repeated measurements of the available water in 30 patients at delivery and in the puerperium. The total loss in available water, from just ante partum to the sixth week post partum averaged 6.1 liters (13.2 pounds), in good agreement with the estimated gain during pregnancy. The loss at delivery was accounted for in the fetus, placenta, amniotic fluid and blood loss. The major decrease, of 2.30 liters (5 pounds) occurred in the first six days of the puerperium.

Freyberg, Reekie and Folsome⁹⁶ determined the water balance by metabolic methods of Newburgh in 53 of the last 62 days of pregnancy

in a young primipara. The total water retention was 6.2 pounds, of which 2.05 pounds were attributed to protein and fat formation (is the stored nitrogen held as protein with the usual proportion of water?—see above). They subtract 2.2 pounds because the patient delivered in the middle of a salt and water excretion test; 0.54 pounds of water is assigned to the fetus, apparently as extracellular water. These corrections leave only 1.4 pounds for hydration of the maternal tissues. However, the interstitial fluid may have increased more than this, because the amniotic fluid was presumably decreasing (Beck), and the blood volume did decrease by 550 ml. Also the patient had a markedly positive sodium balance, gaining 17.12 grams of Na in this period. Unless stored in an osmotically inactive form (as in the bones), sodium is thought to be held extracellularly, and might be expected to withdraw some water from the cells in order to maintain osmotic equilibrium. In comparing this experiment with the measurements of thiocyanate-available water, it should be remembered that thiocyanate is thought to measure only the water outside of the cells (see below). It was suggested by Chesley and Annitto⁷⁵ that some cellular water perhaps does shift out to the interstitial compartment during pregnancy.

Hewitt and Van Liere¹⁰⁴ measured directly the water content of the liver, muscle and skin of guinea pigs. Neither the early or late, nor the early postpartum animals showed any significant difference from the controls. Childs and Eichelberger⁷⁹ determined the distribution and quantities of water and electrolytes in the skeletal muscle of 20 non-pregnant and 10 pregnant dogs. They found no water retention, no shift of water from one compartment to another, and no changes in the electrolytes during pregnancy. In a later paper, Eichelberger, Eisele and Wertzler⁹³ report similar determinations of water and electrolyte distribution in the skins of 3 pregnant dogs as compared with 10 non-pregnant controls. The average water content of the fat-free skins from the pregnant dogs was 752.1 Gm. per kg., as compared with an average of 708.3 Gm. per kg. in the controls. There was also a slight increase in the serum water of the pregnant dogs. Parhon, Cahane and Marza¹²³ found that pregnancy in the guinea pig increased the water content of blood, muscle, and liver. However, the average differences were slight.

TABLE X. THE RELATION OF MAXIMAL DIASTOLIC BLOOD PRESSURE READINGS AND OF EXCESSIVE WATER RETENTION TO THE SUBSEQUENT DEVELOPMENT OF PRE-ECLAMPSIA

| MAXIMAL DIASTOLIC ON ANY OCCASION, MM. HG: | LESS THAN 65 | 66 TO 70 | 71 TO 75 | 76 TO 80 | 81 TO 85 | 86 TO 90 | MORE THAN 90 |
|---|--------------|----------|----------|----------|----------|----------|--------------|
| Cases | 70 | 182 | 154 | 398 | 139 | 171 | 77. |
| Incidence of toxemia in all cases, per cent | 0.0 | 0.5 | 2.6 | 5.0 | 9.4 | 18.1 | 32.5 |
| Incidence of toxemia with normal water at time of test, per cent | 0.0 | 0.6 | 1.6 | 2.2 | 6.3 | 11.5 | 12.2 |
| Incidence of toxemia with excessive water at time of test, per cent | 0.0 | 0.0 | 6.9 | 16.5 | 20.7 | 34.7 | 72.0 |

The negative sodium balances which Taylor and associates¹³³ found in the early puerperiums of their 3 human subjects (Table IX) are of about the magnitude to be expected from the readjustment of the

blood volumes alone. Hummel and associates¹⁰⁵ followed the mineral balance of a nursing multipara from the tenth day to the eighth week postpartum, and found a net retention of 22.27 Gm. of sodium in 43 days of lactation (where could this go?). From these 2 papers, then, there is not any evidence for the post-partum discharge of interstitial fluid gained during pregnancy. On the other hand, Crabtree⁸⁴ did find markedly negative water balances in the early puerperium. In the 8 cases observed for 6 days or more, the negative water balance ranged from 1,830 ml. (4.02 pounds) to 6,330 ml. (13.92 pounds), and averaged 4,440 ml. (9.8 pounds). These figures do not include water lost in milk, feces, lochia, and by transpiration. These last factors bulk considerably larger than does the preformed and metabolic water derived from the food, which factor was not considered by Crabtree. †

These findings in guinea pigs and dogs raise the question as to the validity of the measurements of extracellular water by the thiocyanate method, at least in pregnancy. It is possible that during pregnancy the permeability of some cells may increase so as to admit thiocyanate. If this should happen, the thiocyanate-available water would include not only the extracellular water, but also the water of these cells. Alternatively, the pregnant woman may react differently from the guinea pigs and dogs, as indeed she does in her susceptibility to the pre-eclamptic syndrome. That she does so is strongly suggested by the clinical and physiologic observations detailed above, which point to water retention of about the degree indicated both by the thiocyanate tests, and by Crabtree's data on water losses after delivery. The work of Feldman and associates⁹⁴ indicates that species differences do exist. They found marked dilution of the blood in women and in rats during pregnancy, while the cow showed no such change.

In summarizing all of the components considered in the total weight gain of normal pregnancy, we have: Conception product 11.2 pounds, uterine growth 2.5 pounds, breast growth 3 pounds, protein retention not included in other factors about 4 pounds, blood volume increase 3.5 pounds, interstitial water increase not included in other factors about 4.5 pounds (? from thiocyanate measurements). These factors, which do not include fat gains, give a total, as a rough estimate, of 28.7 pounds which is 4.7 pounds more than the average weight gain (Table I). Elimination of the interstitial water gain would correct the difference, and might be rationalized by discounting the thiocyanate measurements or by considering that much of thiocyanate-available water had merely shifted out of the cells. Such water shifts seem to occur under the influence of the sex steroids.^{80, 119, 145}

Toxic Pregnancy.—The water retention occurring in many cases of pre-eclampsia and eclampsia is too obvious to require discussion. Such edema formation frequently precedes hypertension and other signs of toxemia, and it is this which the clinician is looking for in his routine weighings of obstetric patients.

* The cause of edema formation in incipient pre-eclampsia is unknown. Of the factors considered above in relation to water retention, none can be directly incriminated as the primary cause. 1. The venous pressure seems to be in the range of values found in the nonpregnant and normally pregnant subjects (see McLennan¹¹⁶ for review). 2. The oncotic pressure of the plasma is perhaps a little lower in toxemia than in nor-

mal pregnancy (Table VIII), but most investigators have not regularly found decreases marked enough to account for the palpable edema (see Dieckmann and Kramer⁸⁸ for review). 3. The oncotic pressure of the interstitial fluids is not unduly increased in toxemia. The few determinations of the protein content of edema fluid from toxemic patients have shown concentrations of less than 0.4 Gm. per 100 milliliters^{68, 87, 103, 112, 122}. 4. Changes in capillary permeability are largely unassessed, but cannot be gross as indicated by the low protein content of the edema fluid. McLennan¹¹⁷ found that in edematous toxic patients the rate of filtration from the arm capillaries was less than in normal pregnancy. This, he explains, is probably attributable to the increased interstitial hydrostatic pressure (tissue turgor increased by edema) which opposes filtration. At least, these experiments seem to show that any increase in capillary pressure, decrease in oncotic pressure, and/or increase in capillary permeability are offset by opposing factors. 5. The sodium retention is increased, and in severe toxemia, the urine may be almost sodium-free.^{67, 86, 88} However, this is merely another way of saying that edema is forming. 6. The blood and urine levels of the steroidal hormones are usually diminished in pre-eclampsia.^{129, 131} Taylor has suggested, as an admitted speculation, that such diminution may mean an increased utilization which conceivably could increase the sodium and water retention. 7. Dieckmann⁸⁸ has considered a renal factor in the sodium retention and edema formation—"the renal function is altered if not actually temporarily impaired." Taylor, Warner and Welsh¹³³ point out that the measurements of renal blood flow and glomerular filtration^{78, 83, 90, 110, 134} indicate no disturbance in renal function even in severe toxemia with marked hypertension. Perhaps the steroidal sex hormones act on the renal tubules to increase the reabsorption of sodium from the glomerular filtrate, as do the adrenal cortical steroids.¹⁰²

Of the various components of weight gain in pregnancy, the one factor obviously related to the development of pre-eclampsia is water retention, and whatever value weight-taking may have in the detection of incipient toxemia probably depends upon the correlation between rapid weight gain and edema formation. It is, then, desirable to measure the water content or change in pregnant patients. There is available no generally practicable method for the determination of total body water. However, the extracellular water can be measured roughly by the use of thiocyanate^{85, 114} (also by sucrose,¹¹⁴ sulfate,¹¹⁴ radioactive sodium or chloride,^{107, 144} bromide,¹⁴² or iodide¹⁴²). Practically, this measurement is probably the more valuable, since most edema is largely extracellular.

Chesley and Chesley^{11, 77} determined the thiocyanate-available (roughly extracellular) water in 1,388 patients in the last 10 weeks of pregnancy. At the time of the test, these patients manifested no sign of toxemia. The incidence of subsequent pre-eclampsia in 1,110 patients with normal proportions of available water, *at the time of the test*, was 3.9 per cent. Many of these toxic patients might have been detected had the test been done a second time, since the average time from the normal finding to the appearance of hypertension was six weeks. In 278 patients, (about 20 per cent of the series), having abnormally high proportions of available water, the incidence of the subsequently developing pre-eclamptic syndrome was 22.8 per cent. As done, the test picked out 59 per cent of the future pre-eclamptics (and missed 41 per cent). The test was not very specific in that 77 per cent of the patients selected as potential toxemias did not develop pre-eclampsia.

There were several factors which seemed to predispose to the development of toxemia in the patients with abnormal water retention. The incidence of pre-eclampsia in these patients increased with: 1. Lower serum proteins; 2. greater degree of water retention; 3. longer duration of water retention; 4. greater body weight; 5. higher maximal blood pressure (in upward spikes) occurring at any time, especially at the first clinic visit; 6. history of toxemia in a previous pregnancy.

The test was of little utility in about one-fourth of all patients, since the incidence of excessive water and especially of toxemia was low in patients whose blood pressure had never exceeded 110/70.

The importance of the maximal diastolic blood pressure, as observed at the time of single upward spikes, deserves special mention. Of the normal pregnancies, without regard to water measurements, 73 per cent of patients never showed on any occasion a diastolic pressure as high as 80 mm. Hg. Of the toxic pregnancies, 73 per cent of patients did show diastolic pressures of 80 mm. Hg or more on at least one occasion. Correlating the maximal diastolic pressure readings with the results of the available water measurements enables one to pick out different groups of patients in whom toxemia is highly unlikely to appear, and other groups in whom the toxemia incidence will exceed 70 per cent. This correlation is offered in Table X.

In summary, the causes of edema in pre-eclampsia are unknown. The formation of such edema can be detected early by the measurement of thiocyanate-available water, and many cases of toxemia can thus be picked out in their incipency.

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Correspondence

Manual Dilatation of the Cervix Under Caudal Anesthesia

To the Editor:

In the May issue of the JOURNAL appeared a report by Rosenfeld on five cases of manual dilatation of the cervix under spinal anesthesia and in the August issue there was a comment on this subject by Kassebohm and Schreiber. Like the latter authors, I tried to dilate the cervix under spinal anesthesia but failed to carry out my purpose with the ease claimed for this procedure first by Delmas in 1928, and more recently by others. Doctors Kassebohm and Schreiber referred to the editorial comment I made on Koster and Perrotta's article concerning the Delmas' procedure in the 1943 *Year Book of Obstetrics and Gynecology*. Unfortunately, some physicians are now resorting to the Delmas' method of accouchement forcé and in the hope of dissuading some unskilled ones from attempting to carry out this procedure, may I call attention to my comment which is as follows:

"One of the most pernicious attempts to revive accouchement forcé was made by Koster and Perrotta (*Exper. Med. & Surg.* 1: 143, May, 1943). Koster is a general surgeon, and therefore he is not expected to know much, if anything about obstetrics. I don't know what specialty if any Perrotta practices because I could not find either Koster's or Perrotta's name in the 1942 *Directory of Medical Specialists*. These men report a series of 39 cases in which they took pregnant women before term, gave them a spinal anesthetic and then 'stretched the cervix in various directions until successively two, three and finally four fingers are introduced into it.' After rupturing the membranes, they delivered the baby by forceps or version and extraction.

"In 1928, Delmas of Montpellier, France, advocated exactly the same procedure. The toll of deaths of mothers and babies which followed this monstrous treatment led to abandonment of it. Ostreil (*Zentralb. f. Gynäk.* 58: 325, Feb. 10, 1934), analyzed a series of 120 of these rapid dilatations under spinal anesthesia performed by 30 French obstetricians who reported their results. There were 24 cases of deep cervical lacerations, 2 of complete laceration of the perineum, 2 of ruptured uterus; in 3 cases dilatation could not be carried out, and in 2 cases vaginal cesarean section had to be done. In this series of 120 cases there were 8 maternal deaths and 9 fetal deaths!!

"The majority of obstetricians agree that spinal anesthesia is the most dangerous anesthetic for pregnant women. Koster and Perrotta claim otherwise, but that is their opinion and they are entitled to it. However, with complete and utter disregard for human welfare, these authors say: "Regarding the objection to operative delivery, it must be conceded that it is the price for electively terminating a pregnancy without labor or pain." This is a remarkable attitude for a physician to take. I feel certain that if the dangers of the Delmas' procedure were pointed out to pregnant women, Koster and Perrotta would have very few patients on whose cervixes they would exercise their fingers."

J. P. GREENHILL, M.D.

CHICAGO, ILL.
SEPTEMBER 7, 1944.

To the Editor:

In the August number of the JOURNAL, page 281, Doctors Kassebohm and Schreiber make a passionate attack on the procedure of accouchement forcé. I am just as much opposed to unindicated and indiscriminate accouchement forcé as they are, and in a paper recently read by me before the Obstetrical and Gynecological section of the New York Academy of Medicine entitled "The Place of Rapid Vaginal Delivery Under Spinal Anesthesia," I stated that if this procedure should come to be extensively utilized by general practitioners and young specialists that both the maternal and fetal mortalities and morbidities would rise precipitously. I further stated that if one wishes to retrogress and go back to accouchement forcé, he can perform that procedure almost as well under general as under spinal anesthesia.

They question my statement that under spinal anesthesia, the musculature of the cervix relaxes while the musculature of the corpus contracts. They ask are there muscles in the cervix at term or are there merely some muscle fibers? They also ask why should muscle fibers in one portion of an organ relax when the tonus of the fibers in another portion of the same organ increases.

With reference to the presence of muscle fibers in the nonpregnant cervix, authorities including Stahr, Cunningham and Piersol all agree that the cervix contains muscle tissue, and moreover, that the stratification of the muscle tissue in the cervix is more pronounced than in the corpus.

During pregnancy, most authors of texts are agreed that the cervix contains muscles, though the hyperplasia noted in the corpus is absent. Beck states that the muscle fibers in the cervix diminish in number, but those that remain undergo hypertrophy. Otto H. Schwarz writing in Curtis' system says that the cervix increases in size during pregnancy as a result of the hypertrophy of the muscle fibers just as does the body of the uterus. All authors are in agreement that there is a marked increase in the amount of fibrous, elastic and vascular tissues. So much so that the cervix is practically an erectile organ during pregnancy.

It is hard to conceive that all the above described muscle tissue disappears or is rendered functionless at term or during parturition.

As to nerve innervation, it is well known that systems and organs containing smooth muscle are automatic and that they function despite severance of all extrinsic nerves. Nevertheless, drugs and stimuli acting on the extrinsic nerves influence and largely determine the reactions of these structures.

Pharmacologic and physiologic literature is replete with instances where a given drug will act as a pressor in one section of the intestine and as an inhibitor in another segment. For example, Melville and Stehle have demonstrated that the oxytocic principle of pituitary extract when given to dogs leaves the colon unaffected, causes relaxation of the circular muscle in the small intestine and produces contraction of the longitudinal muscle. None of the contents of the small bowel passes through the ileocecal valve.

Newton, after demonstrating the power of the cervix to contract, showed that the corpus and cervix exhibited not only opposite reactions to adrenalin but that the cervix proved quite insensitive to pitocin. He also showed in rat uteri that the muscles of the horns do not uniformly respond to pitocin.

In the same manner we know that nerves, with wide distribution, carry pressor impulses to some tissues and organs and inhibitory impulses to others. Reynolds in his text *Physiology of the Uterus*, states that aside from the region of the cervix the musculature of the uterus is devoid of a ganglionic nervous system. I quote this passage to show that some difference exists between the nerve patterns of the cervix and the corpus.

Unfortunately, we are ignorant of many of the basic facts underlying the functions of the uterine nerves, but our inability to explain these functions in no way alters them nor does it change their effects.

As to some of the other questions raised by Doctors Kasseholm and Schreiber—"Is it possible to efface the cervix manually?" I don't know as I never tried it at term. I have never attempted manual dilatation unless the cervix was effaced. I did try on one occasion to dilate a cervix manually in early pregnancy (therapeutic abortion) under spinal anesthesia but did not succeed.

When it comes to dilatation of the cervix, certainly the cervix can be dilated manually if by dilatation one means to spread out or make wider.

"Are many of the cervixes lacerated in the performance of manual dilatation?" Yes, but so are they by other methods of delivery. It is well known that a great many lacerations of the cervix occur without most attendants either seeking or being aware of their presence.

"Does the cervix or the internal os become more pliable after spinal anesthesia?" Definitely yes. It makes no practical difference whether this pliability is due to the inhibition of the cervical muscles or changes in the cervical vascular pattern, for admittedly either of these effects would have to be mediated through the nervous system. Cervixes that I was unable to dilate under local and paracervical anesthesia, I was readily able to dilate under spinal. I admit and from personal experience know that manual dilatation can be performed under other forms of anesthesia.

"Do the corporeal muscles contract under spinal anesthesia?" From experience with both vaginal and abdominal delivery under spinal anesthesia, my answer is a categorical yes. The uterine contractions do not cease while the patient is under the influence of the anesthetic. In over one-half of the patients whom I desired to deliver by podalic version, I had to resort to forceps, because the corpus was so tightly contracted proper entrance of the hand into the uterine cavity could not be effected. In two such instances, ether anesthesia was superimposed on the spinal and version was then performed with ease.

I prefer spinal to general anesthesia because with the former the blood loss is greatly diminished, the child cries spontaneously so that resuscitation is rarely required, shock occurs less often and cervical repair is facilitated because the field is so much drier than under general anesthesia.

I believe that the procedure has a very limited field and the indications are few, but when the proper indications are present and if the operation is performed by a competent obstetrician it can save many an infant's life and many hours of maternal travail. It is not a pain-relieving method in the sense that caudal anesthesia is, and it should not be so employed.

In conclusion, I do not believe that truth can be successfully scotched. Let us rather thoroughly discuss and compare experiences rather than bury a method that admittedly is useful in trained hands. It would be just as logical to "forget about" forceps and versions because incompetents might attempt these beautiful and lifesaving procedures. Let us rather train our doctors so that they may be competent obstetricians and at the same time educate the public so that they demand expert service.

SAMUEL S. ROSENFELD, M.D.

NEW YORK, N. Y.

SEPT. 5, 1944

Society Transactions

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF MAY 5, 1944

The following papers were presented:

Hemorrhage as the Most Important Cause of Maternal Death in Brooklyn in 1943. Charles A. Gordon, M.D., (For original article, see page 557.)
Personal Recollections of Dr. Joseph B. DeLee. J. P. Greenhill, M.D.

Item

American Board of Obstetrics and Gynecology, Inc.

A number of changes in Board regulations and requirements were put into effect at the Board's last annual meeting. These were designed to aid civilians as well as candidates in the Service. Among these is the waiver, temporarily, of the A.M.A. requirement for men in the Army or Navy, especially for those who proceeded directly or almost so from hospital services into Army or Navy Service, upon a statement of intention to join promptly upon return to civilian practice. At this meeting the Board decided also to accept a period of nine months as an academic year in satisfying our requirement for certain years of training. This is only for the duration and even men who are not eligible for Military Service but who are nevertheless in hospitals where the accelerated program is in effect have been allowed to submit to us this short-time period of training in lieu of our previous requirements.

Beginning with the next written examination, which is scheduled to be held the first Saturday afternoon in February, 1945, this Board will limit the written examination to a maximum period of three hours and in submitting case records at this time, all obstetric reports which do not include measurements either by calipers and, as indicated, by acceptable x-ray pelvimetry, will be considered incomplete.

Prospective applicants or candidates in Military Service are urged to obtain from the Office of the Secretary a copy of the "Record of Professional Assignments for Prospective Applicants for Certification by Specialty Boards" which will be supplied upon request. This record was compiled by the Advisory Board for Medical Specialties and is approved by the Offices of the Surgeons-General, having been recommended to the Services in a circular letter, No. 76, from the War Department Army Service Forces, and referred to as the Medical Officer's Service Record. These will enable prospective applicants and candidates to keep an accurate record of work done while in Military Service and should be submitted with the candidate's application, so that the Credentials Committee may have this information available in reviewing the application.

Applications and BULLETIN of detailed information regarding the Board requirements will be sent upon request to the Secretary's Office, 1015 Highland Building, Pittsburgh, 6, Pennsylvania. Applications must be in the Office of the Secretary by November 15, 1944, ninety days in advance of the examination date. The time and place of the Spring 1945 (Part II) examination will be announced later.

PAUL TITUS, M.D.

1015 HIGHLAND BUILDING,
PITTSBURGH, 6, PA.

The following physicians have recently completed our requirements and have now been certified by the American Board of Obstetrics and Gynecology:

Burkons, Harold F. M.D., 1170 Everglades Concourse, Miami Beach, Fla.

Kantor, Herman I. M.D., MDETS, Billings General Hospital, Fort Benjamin Harrison, Ind.

Stern, Alfred, M.D., 355 30th Street, Oakland, Calif.

Wolff, Frederick Siegfried, Captain (MC), MDETS, Fort Snelling, Minneapolis, Minn.

PAUL TITUS, M.D.

Secretary.

Necrology

FREDERICK CLARK HOLDEN, M.D., D.P.H. (Hon.), Director of Gynecology at the Jersey City Medical Center and Professor Emeritus of Obstetrics and Gynecology at the New York University Medical School, past President of the American Gynecological Society, the New York Obstetrical Society, and consultant in several hospitals, long a resident of New York City, died suddenly at Prout's Neck, Maine, on August 27, in the 75th year of his age.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

- American Gynecological Society.** (1876) *President*, Edward A. Schumann, Philadelphia, Pa. *Secretary*, Howard C. Taylor, Jr. 842 Park Ave., New York, N. Y. Next annual meeting, June, 1945.
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons.** (1888) *President*, Lewis F. Smead, Toledo, Ohio. *Secretary*, James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 1944.
- Central Association of Obstetricians and Gynecologists.** (1929) *President*, John H. Moore, Grand Forks, N. D. *Secretary-Treasurer*, W. F. Mengert, Dallas, Tex. Annual meeting not announced.
- South Atlantic Association of Obstetricians and Gynecologists.** (1938) *President* Oren Moore, Charlotte, N. C. *Secretary*, T. J. Williams, University, Va. Annual meeting cancelled.
- A. M. A. Section on Obstetrics and Gynecology.** *Chairman*, Philip F. Williams, Philadelphia, Pa. *Secretary*, William Mengert, 2211 Oak Lawn Ave., Dallas Tex. Next meeting, New York City, June, 1945.
- New York Obstetrical Society.** (1863) *President*, W. E. Studdiford. *Secretary*, R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.
- Obstetrical Society of Philadelphia.** (1868) *President*, Charles A. Behney *Secretary*, John B. Montgomery, Pro tem, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.
- Chicago Gynecological Society.** (1878) *President*, William J. Dieckmann. *Secretary*, Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.
- Brooklyn Gynecological Society.** (1890) *President*, James P. McManus. *Secretary*, William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.
- Baltimore Obstetrical and Gynecological Society.** (1929) *President*, Lawrence Wharton. *Secretary-Treasurer*, John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.
- Cincinnati Obstetrical Society.** *President*, Edward Friedman. *Secretary*, Carroll J. Fairo, Cincinnati, Ohio. Third Thursday of each month.
- Louisville Obstetrical and Gynecological Society.** *President*, Layman A. Gray. *Secretary*, E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.
- Portland Society of Obstetrics and Gynecology.** *President*, Howard Stearns. *Secretary*, William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.
- Pittsburgh Obstetrical and Gynecological Society.** (1934) *President*, H. A. Power. *Secretary*, Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.
- Obstetrical Society of Boston.** (1861) *President*, Thos. Almy, Fall River, Mass. *Secretary*, Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.

*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the name is the year of founding.

- New England Obstetrical and Gynecological Society.** (1929) *President*, Roy J. Hefferman, Brookline, Mass. *Secretary*, Fred J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.
- Pacific Coast Obstetrical and Gynecological Society.** (1931) *President*, T. Floyd Bell. *Secretary-Treasurer*, William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.
- Washington Gynecological Society.** (1933) *President*, James R. Costello. *Secretary*, J. Keith Cromer, 1835 Eye St., N.W., Washington, D. C. Fourth Saturday, October to May.
- New Orleans Obstetrical and Gynecological Society.** (1924) *President*, E. L. Zander. *Secretary*, R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.
- St. Louis Gynecological Society.** (1924) *President*, S. A. Weintraub. *Secretary*, Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Meetings second Thursday, October, December, February, and April.
- San Francisco Gynecological Society.** (1929) *President*, R. Glenn Craig. *Secretary*, D. G. Morton, California University Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.
- Texas Association of Obstetricians and Gynecologists.** (1930) *President*, T. F. Bunkley. *Secretary*, J. McIver, 714 Medical Arts Bldg., Dallas, Tex.
- Michigan Society of Obstetricians and Gynecologists.** (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, Norman F. Miller. *Secretary*, Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).
- Obstetric Society of Syracuse Hospitals.** (1938) *President*, Edward C. Hughes. *Secretary*, Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May. Suspended for the duration.
- Alabama Association of Obstetricians and Gynecologists.** *President*, J. M. Weldon, Mobile, Ala. *Secretary*, Eva F. Dodge, Montgomery, Ala.
- San Antonio Obstetric Society.** *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.
- Seattle Gynecological Society.** (1941) *President*, R. Philip Smith. *Secretary*, Gerhard Ahnquist, 1336 Madison Street, Seattle. Meetings held on third Wednesday of each month.
- Denver Obstetrical and Gynecological Society.** (1942) *Secretary*, Emmett A. Meehler, 1612 Tremont St., Denver, Colo. Suspended during war.
- Wisconsin Society of Obstetrics and Gynecology.** (1940) *President*, Roland S. Cron. *Secretary*, Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.
- San Diego Gynecological Society.** (1937) *President*, Geo. D. Huff. *Secretary*, Frank Russell, 233 A St., San Diego, Calif. Meetings held on the last Wednesday of each month.
- North Dakota Society of Obstetrics and Gynecology.** (1938) *President*, Ralph E. Leigh, Grand Forks. *Secretary*, G. Wilson Hunter, 807 Broadway, Fargo, N. D.
- Virginia Obstetrical and Gynecological Society.** (1936) *President*, A. L. Carson, Jr. *Secretary*, L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.

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Original Communications

OVARIAN FIBROMAS AND THECA-CELL TUMORS: REPORT OF 78 CASES WITH SPECIAL REFERENCE TO PRODUCTION OF ASCITES AND HYDROTHORAX (MEIGS' SYNDROME)*†

I. C. RUBIN, M.D., F.A.C.S., J. NOVAK, M.D., AND J. J. SQUIRE, M.D.,
NEW YORK, N. Y.

(From the Gynecological Service of Mount Sinai Hospital)

THE association of ascites with hydrothorax was observed as far back as 1879, when Cullingworth reported a case.¹ Its clinical importance and practical implications, however, were not appreciated until Meigs and Cass² called special attention to the syndrome since become known as the Meigs' Syndrome. In 1885, Terrier,³ stressed that ascites does not indicate malignancy in every case. Since the publication by Meigs et al., the occasional occurrence of ascites has been noted in connection with other benign ovarian tumors such as myomas, fibroadenomas, benign seropapillary cystomas and struma ovarii.

The object of the present report was first to analyze the cases of ovarian fibromas and theca-cell tumors encountered in the gynecologic material of Mount Sinai Hospital with special reference to the incidence of ascites and hydrothorax, and secondly to determine, if possible, how these effusions are produced.

The comparatively frequent association of ascites with ovarian fibromas has been recognized by gynecologists for a long time. Statements concerning the frequency of its occurrence, however, differ considerably. Kermauner,⁴ for example, had only one case of extensive ascites in his large material, whereas other authors found its occurrence in 40 to 50 per cent of their cases. This great difference may be explained by the statistical error of small numbers on the one hand, and by the selection of the material on the other. Authors who have pub-

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lished a high percentage of ascites in their own series, for example Lippert⁵—72 per cent, Stuebe⁶—50 per cent, Peterson⁷—40 per cent, most probably did not include the cases of small fibromas.

Incidence.—In the period between 1928 and 1943 (inclusive), 78 cases of fibromas and theca-cell tumors were encountered in the Mount Sinai Hospital. Theca-cell tumors were included in our statistics because (1) they typify Meigs' syndrome as well as the fibromas; and (2) because in the period between 1928 and 1936, no distinction was made in the pathologic reports between these two kinds of tumors. Since 1936, every ovarian tumor of connective tissue variety was stained for fat, and the fat content has been regarded as an important characteristic of theca-cell tumors in differentiating them from fibromas.

The first group of tumors (from 1928 to 1936) consists of 23 cases. In 7 cases, the tumors were small, measuring at most 5 cm., in 10 cases, they were of medium size (from hen-egg to apple size); in 5 cases, they were large (bigger than an average-sized grapefruit). In one case, there was no definite note as to size. Ascites was observed in 9 cases of this group. In two the amount of fluid was small, in three moderate, and in four considerable. In six cases with ascites, the tumors were of large size, and in three they were of medium size. In seven cases, the tumors were edematous and, for the most part, cystic; in two cases they were hemorrhagic. Hydrothorax was met in only one case of this group. The pleural effusion was bilateral and much more pronounced on the right side than on the left. It was hemorrhagic whereas the ascitic effusion was described as amber colored. This unusual circumstance is not explained.

TABLE I

| | | | | |
|--|----------------------|----|---------------|---|
| Size of tumor | Small | 7 | | |
| | Medium | 10 | | |
| | Large | 5 | | |
| Amount of fluid (9 cases of ascites) | Small | 2 | SIZE OF TUMOR | |
| | | | Large | 1 |
| | | | Medium | 1 |
| | Moderate | 3 | Large | 2 |
| | | | Small | 1 |
| | Considerable | 4 | Large | 2 |
| | | | Medium | 2 |
| Condition of tumor in the 9 cases of ascites | Edematous and cystic | 7 | | |
| | Hemorrhagic | 2 | | |

From this table it is seen that the amount of ascites does not depend altogether on the size of the fibroma.

The second group consists of 30 fibromas (including fibromyomas), 2 cases of papillary fibro-adenoma and 23 cases of theca-cell tumor. This fairly large group indicates incidentally that theca-cell tumors are not as rare as has been generally assumed. Three of the fibromas were large, 14 of medium size, and 13 small. There was a small amount of ascites in only 2 of the fibroma cases. The relative infrequent occurrence of ascites in this group is difficult to account for. In one of the two cases of papillary fibro-adenoma which we would prefer to include among the sero-epithelial rather than among the fibromatous growths, a small amount of ascitic fluid was found at operation. Hydrothorax was not found in any of these 30 cases of ovarian fibroma,

TABLE II

| TYPE OF TUMOR | NUMBER | SIZE | | |
|------------------------|--------|-----------------|----------|--------------|
| | | SMALL | MEDIUM | LARGE |
| Fibroma | 30 | 13 | 14 | 3 |
| Papillary fibroadenoma | 2 | 1 | 0 | 1 |
| Theca cell | 23 | 8 | 11 | 4 |
| | | AMOUNT OF FLUID | | |
| | | SMALL | MODERATE | CONSIDERABLE |
| | | 0 | 4 | 3 |

Among the 23 cases of theca-cell tumors, ascites was noted seven times. The abdominal effusion was extensive in 3 cases with large tumors. A right-sided hydrothorax associated the ascites in one case. In 4 cases with a moderate amount of ascitic fluid, the tumors were only of medium size, i.e., from that of a hen's egg to the size of a grapefruit. In 6 cases with ascites, the newgrowths were edematous, in 4 cases cystic.

Thus, it is evident that theca-cell tumors are not infrequently accompanied by ascites (in 30 per cent of our material), and also that Meigs' syndrome may also be met in this class of tumors of the ovary. Since no distinction was formerly made between fibromas and theca-cell tumors, some of the "fibromas" with Meigs' syndrome mentioned in the literature may have actually been theca-cell tumors.

Clinical Significance of Ascites in Relation to Ovarian Tumors in General

Ascites, which is commonly found in the presence of ovarian tumors, as a rule, indicates the spread of malignancy to the peritoneum. In such cases, the origin of the ascitic fluid is easily understood. It is partially a wound secretion of the disintegrating tumor, and partially an exudate of the peritoneum which is irritated by the presence of the tumor. Frequently, the irritative condition is recognized by the intensive redness of the peritoneum, which may be present in areas not as yet involved in the malignant growth.

Pseudomyxoma and papilloma of the ovary produce peritoneal implantation, and though histologically not malignant, they assume an intermediate position between benign and malignant tumors, and produce in each case a similar type of ascites. Torsion of the pedicle, necrosis and inflammation may produce ascites in benign as well as malignant tumors. The amount of intraperitoneal effusion under these circumstances is usually scant. If we exclude these cases, then the presence of an ovarian tumor with a considerable effusion usually indicates malignancy and peritoneal spread. Dermoid cysts and pseudomucinous cysts are only exceptionally accompanied by ascites, a fact recognized by gynecologists for a long time; and the more recently described Brenner tumors are never associated with ascites.

In reviewing John Miller's^s large collection, from various sources, of 2,748 ovarian tumors, we noted that ascites was present in 6 per cent of the benign and in 45.8 per cent of the malignant ovarian tumors.

However, these figures should be viewed with caution, since on the one hand, notes on small amounts of peritoneal effusion are frequently omitted in the clinical records and, on the other hand, cases of twisted ovarian tumors and inflammation might have been included.

Origin of Ascites.—The problem of the origin of the ascitic fluid is still unsolved. Attempts to explain its origin on a mechanical basis or chemical irritation of the peritoneum (Olshausen,⁹ Pfannenstiel,¹⁰ Shoer,¹¹ et al.) have not been satisfactory. No convincing evidence of such irritation was adduced. Neither the composition of the ascitic fluid, nor the anatomicopathological condition of the peritoneum as observed in the limited number of cases where special attention was paid to these two factors, confirmed the assumption of a peritoneal irritant. The idea that there may be a causal relation between the abdominal effusion and Selye's¹² "alarm reaction" is, in our opinion, not justified. This is in accord with the opinion held by Meigs. The "alarm reaction" is a response of the organism to an irritant to whose qualitative and quantitative effects the organism is not accustomed. That ovarian fibroma does not produce ascites by its mere presence within the peritoneal cavity is borne out by the fact that uterine fibroids, despite their size, similarity in structure and degenerative changes cause ascites only in very rare cases. Kelly and Cullen¹³ reported seven such cases, one of them with pleural effusion as well, and a similar case was published from Dr. R. T. Frank's Service at Mount Sinai Hospital.¹⁴

A more acceptable theory is that which has been offered by Spencer and Miller, namely, that the ascitic fluid may originate from the tumor itself. Miller⁸ quotes as proof of his belief a very interesting observation of Geibel.¹⁵ This author put the tumors of his two cases into a completely dry pot. After a few hours, the vessel was filled with clear, yellowish fluid. After 24 hours, one of the tumors, which measured 20 by 15 by 12 cm. and weighed 3,200 Gm. with the exuded fluid, weighed 2,050 Gm. without the fluid. Thus, it lost about one-third of its weight within 24 hours.

How can one explain the discharge of the fluid from the tumor? It is noteworthy that in all the reported cases of Meigs' syndrome in which the pathological histology of the tumors is described, special mention is made of edema, liquefaction and cyst formation. However, similar changes may be present in tumors which are unassociated with ascites. Unfortunately, however, no differentiation has been made in the reported cases between cyst formation (true liquefaction) and extreme edema or cystic dilatation of lymph spaces. Liquefaction and edema are different conditions. Liquefaction refers to dissolution of necrotic tissue. Edema on the other hand, is an accumulation of intercellular fluid which or may not be followed by nutritional disorders or necrosis of the edematous tissue.

In connection with the pathological degeneration of the ovarian fibroma as a possible cause of ascites, it is interesting to recall H. Spencer's¹⁶ discussion in 1906, of Amand Routh's¹⁷ case of an ovarian

fibroma with ascites. Spencer stated that it was a difficult point to determine the cause of ascites in "ovarian fibroids." He had met with one case in which a bleb half an inch thick appeared on the surface of an "ovarian fibroid" and, by squeezing the periphery of the tumor with the hands, fluid could easily be made to ooze from a slight crack in the bleb. This led him to think that in at least some of the cases, the escape of fluid was due to pressure of the hard tumor on the lymphatics or blood vessels in the hilum of the ovary, which Poirrier and others had shown to be so large and numerous.

Considering the fact that the tumor is fibromatous, it is conceivable that constriction of the efferent lymph or blood vessels may take place in the tumor itself or in its pedicle, and thus produce congestion and lymph stasis which may be followed by exudation of tissue fluid on its surface.

Also, in connection with this subject, the question naturally arises as to why ovarian fibromas produce ascites so commonly, while uterine fibroids so rarely, even though both tumors have a similar parenchymatous histological structure and undergo similar circulatory and degenerative changes. The explanation may be found in the fact that uterine fibroids as a rule, are covered by a fibromuscular, dense capsule and invariably by a serosal layer, whereas ovarian fibromas do not have such a capsule, and like the normal ovary, no peritoneal cover. Instead of a true serosa, ovarian fibromas are covered by a low, single layered, very vulnerable and easily permeable surface epithelium which offers practically no resistance to the penetration of fluid from the ovarian tumor.

Bearing this in mind, it would be highly desirable in every case of ovarian fibroma, and particularly in cases with ascitic effusion, to note carefully the condition of the lymph and blood vessels of the tumor as well as the condition of the tumor surface. Injection of the vessels of the specimen might be helpful in revealing more detailed information.

Origin of Hydrothorax.—The origin of ascites in ovarian fibromas challenged inquiry as to its mechanism from the first observations that were made of this combined condition. But even more difficult and challenging was the explanation as to why the ascites was in some cases accompanied by a right-sided, and more rarely by a left-sided or bilateral pleural effusion. Reports of the combination of ascites and hydrothorax in benign tumors are found in the older literature. In 1909, Kelly and Cullen¹³ observed this syndrome in a case of uterine fibroids. In 1914, Caro¹⁸ mentioned its occurrence in giant fibroma of the ovary.

But these observations remained unknown not only to the majority of the medical profession, but also to most gynecologists. Cases with this syndrome were regarded as inoperable and incurable and were, as a rule, treated with repeated paracenteses only. The greatest credit, therefore, is due Meigs for calling attention to the occurrence of ascites and hydrothorax in benign ovarian tumors, and in stressing its clinical

and practical importance. In 1943, Meigs, Armstrong and Hamilton¹⁹ collected 27 such cases from their own material and from the medical literature of this country. In this collection, 18 had pleural effusion on the right side, 4 on the left, and 4 on both sides. In one case, there of this paper, Healy, Herrick and Watson, and Taylor added three other is no note about the location of the pleural effusion. In the discussion cases.

How can we explain the origin of the hydrothorax? And why does it occur on the right side in the great majority of cases? We made these questions the subject of an experimental and clinical study. The following considerations have appeared to us to be basic:

1. Within a few days, the pleural effusion completely and definitely disappears after the removal of the ovarian tumor, therefore, it is a direct result of the tumor and not of an independent or coexistent pleural disease.

2. As stated by Meigs in two cases, the pleural effusion has the same properties as the ascitic fluid. This justifies the conclusion that the pleural effusion originated in the abdomen and was transmitted to the pleural cavity.

3. In the few cases where the effusions were examined, they were poor in cells and had a low specific gravity—1.012 to 1.018, and only exceptionally higher. Thus, they have the characteristics of transudates and not of exudates.

4. The anatomic route by which fluid can be transferred from the abdomen into the pleura was identified a long time ago. As early as 1862 von Recklinghausen²⁰ described small openings between the endothelial cells of the diaphragmatic peritoneum which connect the subperitoneal lymph chain of the diaphragm with the subpleural lymph channels and called them stomata. Later on the correctness of von Recklinghausen's statements was, with some slight differences, affirmed by the majority of investigators. Anatomical studies reported by Kuettner,²¹ Bartels,²² Muscatello,²³ Sulzer,²⁴ Drinker and Yoffey,²⁵ and more recently by Allen,²⁶ Higgins and co-workers²⁷ show that both diaphragmatic surfaces except the tendinous center are rich in lymph vessels. Each half of the diaphragm forms a separate lymph sphere which has only scant connections with that of the other side. The right lymph network is by far better developed than the left. Both subperitoneal lymph networks communicate with the corresponding subpleural lymph networks through perforating vessels. The lymph is removed by five routes according to Higgins and Graham:²⁷ (1) The main route or the sternal route consists of 3 to 4 channels which course along the diaphragm between the intercostal muscles and run forward parallel to the thoracic artery and vein; (2) the pulmonary route consisting of vessels which carry lymph to the nodes at the hilum of the lungs; (3) vessels which run to the thoracic duct; (4 and 5) vessels that pass over the dorsal surface of the diaphragm, pierce it and empty their lymph into the renal and the pancreatic lymph nodes.

Experimental works of von Recklinghausen,²⁰ MacCallum,²⁸ Sulzer,²⁴ Lemon and Higgins²⁹ and others have shown that fluid and small corpuscular particles like India ink, carmine, and black lead pass through the diaphragm within a few minutes and that accumulations of these particles mark the location of the stomata. Clairmont and Haberer³⁰ demonstrated in 1905, that resorption from the peritoneal cavity of a solution of potassium iodide was much delayed after applying collodion over the diaphragmatic peritoneum. A similar delay of resorption of indigo carmine was shown in 1911 by Rubin,³¹ after resecting the omentum in cats suggesting that this anatomic structure may play a role in transporting fluids toward the diaphragm.

In its transference from the subperitoneal to the subpleural lymph vessels the ascitic fluid follows the normal current directed toward the heart. But the intensity and velocity of this flow depends mainly on the respiratory action of the diaphragm which not only exerts a pump effect on fluid situated on the surface of the liver, but also considerably influences the width of the diaphragmatic stomata (Florey, Allen, et al.³²). Paralysis of the diaphragm, according to Higgins, Beaver and Lemon,³³ considerably retards the transference of corpuscular elements but does not prevent it completely.

Considering all these facts, we are not surprised to find ascitic fluid in the pleura but wonder why it does not happen in every case of ascites. The following possibilities may account for it:

1. Rapid absorption of the fluid entering the pleura, thus preventing an accumulation of fluid in the pleural cavity.
2. Slow penetration of the fluid through the diaphragm so that it is absorbed by the pleura with the same speed as it takes to reach it.
3. Blockage of the diaphragmatic stomata by debris or obliteration of the stomata by chronic inflammatory changes of the peritoneum.
4. High osmotic pressure of the colloidal ascitic fluid counteracting the transudation of water. This possibility holds in pseudomyxoma where the myxomatous masses not only do not give up any water, but rather attract and adsorb some.

Experimental Data

We tried to evaluate the action of each of these factors in the production of Meigs' syndrome experimentally on rabbits, rats and mice.

In the first group of experiments, saline stained with carmine or India ink was injected into the abdomen once or repeatedly, and the fluid content of the abdominal and pleural cavities was examined after various intervals.

In a second group, human serum stained with carmine was used instead of saline.

In a third series of experiments, an attempt was made to block the diaphragmatic stomata and the other peritoneal lymph drainage areas by injecting a suspension of kaolin 2 to 3 days before serum was injected.

GROUP I

| NAME AND NO. | AGE | STATUS | OVARIAN PATH. | DETAILS OF PATH. | OTHER PATH. | ASCITES | HYDRO-THORAX | CHIEF COMPLAINTS | SIZE |
|---------------|-----|--------|--|---|---|---|-------------------------|---|--------|
| S. A. 340217 | 57 | M | Fibroma l. ovary | Edematous with cystic degeneration | Cholilithiasis | Small amount of free, clear yellow fluid | None | Enlargement of abdomen | Large |
| L. B. 309645 | 38 | M | Fibroma l. ovary | Hemorrhage and necrosis 20 by 25 by 14 cm. | - | Large quantity of bloody fluid | None | Feels unwell, chilly | Large |
| T. B. 238019 | 49 | M | Fibroma | Edematous, grapefruit size areas of great cellularity and vascularity | Uterine fibroids | Large quantity (about 1 gal.) clear fluid | None | - | Medium |
| M. C. 337216 | 52 | M | Fibroma r. ovary 20 by 15 by 10 | Edematous, partial necrosis | - | 16 to 18 oz. amber colored | 14,000 c.c. r. 500 c.c. | Irregular l. menses Enlargement of abdomen | Large |
| B. G. 387833 | 55 | M | Fibroma l. ovary size of grapefruit | Cystic degeneration | - | None | None | Pain in abdomen | Medium |
| S. G. 373902 | 65 | M | Fibroma l. ovary 3 to 4 cm. diameter | Theca cell origin? | Huge multilocular serous cystadenoma | None | None | Pressure symptoms Albuminuria Edema of legs | Small |
| A. G. 825101 | 37 | M | Bilateral ovarian fibroma: l. 2½ cm. diam., r. 2 by 1 by 1 | - | - | None | None | - | Small |
| S. G. 330090 | 18 | S | Fibroma l. ovary | Degeneration and cyst formation | Small r. ovarian cyst, "called" cystadenoma | About 1,000 c.c. of sanguineous fluid | None | Lower abdominal pain | Small |
| J. H. 3367809 | 21 | S | Fibroma r. ovary | 6 by 4 cm. (orange) cystic degeneration | - | Small amount with yellow tint | None | Metrorrhagia | Medium |
| J. H. 294517 | 39 | Sep. | Fibroma of ovary side? r.? | Small | Chronic appendicitis | None | None | Periodic attacks of pain in R.L.Q. | Small |
| R. L. 312472 | 49 | S | Fibroma r. ovary 24 by 14 by 10 | Twisted, hemorrhagic | - | Moderate amount hemorrhagic twisted pedicle | None | Pain in r. side and back Vomiting | Large |
| M. J. 346886 | 34 | M | Small (hazelnut) fibroma r. ovary | Very firm | r. hydrosalpinx Perioophoritis | None | None | Bleeding Headache Lower backaches | Small |

| R. L. | 59 | M | Small calcified fibroma of a gyrate ovary (nodule about size and shape of "os-magnum") | Small calcified nodule | Acute appendicitis | None | None | Symptoms of appendiceal abscess | Small |
|--------|----|---|--|--|--|---|------|--|--------|
| 312773 | | | | | | | | | |
| H. M. | 40 | M | Fibroma r. ovary 5½ by 3½ cm. | Completely encapsulated, very firm, very cellular | Uterine fibroids | None | None | Pain on r. side, dysmenorrhea, menorrhagia | Medium |
| J. M. | 35 | M | Fibroma r. ovary 3½ by 1½ cm. | Very hard, nodular | Chronic appendicitis | None | None | Amenorrhea 7½ years | Small |
| B. O. | 53 | M | Fibroma and adenocystoma r. ovary | Gangrene caused by torsion (melon-size) | Uterine fibroids | None | None | - | Medium |
| B. R. | 28 | M | Fibroma l. ovary 13 by 9 | Narrow pedicle, fib. encapsulated, gray-yellow on cross section Edematous, very cellular, small cysts | Uterine fibroids Pregnancy | Large amount of ascitic fluid in pelvis | None | Pain in lower pelvis | Medium |
| S. R. | 35 | M | Fibroma r. ovary | - | Uterine fibroids | None | None | Gradual enlargement of abdomen | ? |
| D. R. | 59 | M | Fibromas r. ovary 6 cm. in diameter | Luteum cyst with thickened wall. Twisted? | - | None | None | Pain in lower r. side | Medium |
| S. R. | 30 | S | Bilateral ovarian fibromas 1. 3.5 cm. diam. 2. 13 cm. diam. | 1. Intensely hard, nodular, yellowish areas 2. Cystic | - | None | None | Pain in back | Medium |
| E. U. | 62 | M | Fibroma of ovary 12 by 9 by 8 | Smooth on section Fibrous, creamy white | Small cyst with clear fluid on surface | None | None | - | Medium |
| M. W. | 39 | M | Fibroma r. ovary size of fist | Cellular, yellowish discoloration on cut surface | Pregnancy | None | None | Pain R.I.Q. for 2 weeks | Medium |
| B. W. | 45 | M | Fibroma r. ovary size honey dew melon | Firm, hard, dense, white edematous tissue | - | Moderate amount | None | - | Large |

GROUP II. FIBROMAS

| NAME AND NO. | AGE | STA-TUS | OVARIAN PATH. | DETAILS OF PATH. | OTHER PATH. | ASCITES | HYDRO-THORAX | CHIEF COMPLAINTS | SIZE |
|--------------|-----|---------|----------------------------|---|---|-------------------------------------|--------------|---------------------------------------|--------|
| A. A. 459713 | 16 | S | | | Necrotic endometrial polyp | 1 oz. clear amber-colored | None | - | Medium |
| S. A. 480993 | 22 | S | Fibroma l. ovary | l. ovary—follicular cysts Nodule 3 mm. in diameter | - | None | None | Pain in r. lower abdomen | Small |
| S. A. 457361 | 34 | M | Fibroma l. ovary | l. grapefruit | Small uterine fibroid | None | None | Pain lower abdomen | Medium |
| R. A. 500193 | 50 | M | Fibroma | Small papillomas l. ovary | Uterine fibroids | None | None | Menorrhagia | Small |
| J. C. 492028 | 34 | M | Fibroma r. ovary | r. prune-sized | Uterine fibroid | None | None | Profuse periods | Small |
| S. C. 432560 | 50 | M | Fibroma r. and l. ovary | Large ovary l. 23 by 15 by 15; small r. | Parovarian cyst | None | None | Menorrhagia back pain | Large |
| L. C. 18158 | 76 | M | Fibroma l. ovary | l. ovary cystic fibroma 7 by 6 by 4 cm. | - | None | None | L.L.Q. pain | Medium |
| M. D. 416758 | 32 | M | Fibromyoma 7 by 4 by 2 cm. | Cystic | Seroepithelial cysts | None | None | - | Medium |
| C. E. 354389 | 45 | M | Fibroma r. ovary | Size of grapefruit; l. ovary small | Uterine fibroids | Small amount of amber-colored fluid | None | Amenorrhea L.L.Q. pain | Medium |
| B. F. 438524 | 30 | S | Fibroma | Small—pea-sized | Uterine fibroids | Small amount | None | Constipation Nervous | Small |
| G. F. 353843 | 16½ | S | Fibroma | r. small cantaloupe, l. plum | - | None | None | Amenorrhea Lower abdominal discomfort | Medium |
| S. F. 492628 | 44 | M | Fibroma r. ovary | Small 2 by 2 by 1 cm. | Uterine fibroids Small serous ovarian cyst | None | None | Pressure in pelvis | Small |

| | | | | | | | | | |
|--------------------|----|---|-------------------|--|-------------------------------------|------|------|--|--------|
| I. G. 443002 | 52 | M | Fibroma | l. ovary fibroma small (2½ cm. di- ameter) | Uterine fibroids | None | None | Severe menor- rhagia | Small |
| O. K. 440953 | 65 | M | Fibroma r. ovary | 30 cm. diameter | Follicular cysts l. ovary | None | None | Loss of weight Increase in size of abdomen | Large |
| A. K. 440820 | 36 | M | Fibroma | Plum-sized | Uterine fibroids, endometriosis | None | None | Menorrhagia Profuse flow Clots | Small |
| P. K. 501138 | 51 | M | Fibroma r. and l. | R. 5 by 3. 5 by 3 L. 2 tumors, 10 by 6 by 7, 12 by 9 by 4 cm. | - | None | None | L.L.Q. pain Fullness and press- ing in abdomen | Medium |
| L. K. 444115 | 46 | S | Fibroma r. ovary | Large 14 by 10 by 10 cm. | Uterine fibroids | None | None | Metrorrhagia Lower abdominal pain | Medium |
| E. L. 441652 | 37 | S | Fibroma | R. ovary (10 cm.) diameter | Follicular cysts | None | None | Pelvic mass | Medium |
| R. L. 480685 | 48 | M | Fibroma r. and l. | Small | Uterine fibroids | None | None | Profuse periods bimonthly | Small |
| L. G. M. 355199 | 35 | M | Fibroma | R. ovary | Dermoid cyst l. ovary | None | None | Chronic appendi- citis | ? |
| K. M. 456598 | 52 | M | Fibroma r. ovary | Grapefruit | Uterine fibroids | None | None | Metrorrhagia | Medium |
| E. N. 482232 | 68 | M | Fibroma r. ovary | Small fibroadenoma r. huge serous cyst and fibroad- enoma | Uterine fibroids | None | None | Lower abdominal pain | Small |
| I. P. 478844 | 43 | M | Fibroma r. ovary | Small adenofibroma | Uterine fibroids | None | None | Menometrorrhagia R.L.Q. pain | Small |
| A. S. 422485 | 58 | M | Fibroma l. ovary | L. 12 cm. R. Shrunken | Uterus atrophic | None | None | L.L.Q. pain | Medium |
| E. S. 503564 | 50 | M | Fibroma side? | 5 cm. diameter | Bilateral ovarian adenocarcinoma | None | None | L.L.Q. pain, pres- sure in rectum | Medium |

GROUP II. FIBROMAS—CONT'D

| NAME AND NO. | AGE | STA-TUS | OVARIAN PATH. | DETAILS OF PATH. | OTHER PATH. | ASCITES | HYDRO-THORAX | CHIEF COMPLAINTS | SIZE |
|-----------------|-----|---------|------------------|---|------------------------------------|---------|--------------|--|--------|
| Z. S. 492242 | 50 | S | Fibroma l. ovary | Small | Uterine fibroids, endometriosis | None | None | Feels a tumor in stomach | Small |
| R. S. 380454 | 25 | S | Fibroma l. ovary | Pedunculated 15 by 13 by 8 cm. with numerous small cysts | - | None | None | Pain in lower ab- domen | Large |
| F. S. 488742 | 47 | S | Fibroma r. ovary | Small fibromyoma 2 by 1.5; l. ovary normal | Cyst r. ovary Uterine fibroids | None | None | Mass | Small |
| L. S. 486409 | 50 | M | Fibroma r. ovary | Partially solid and cystic | Uterine fibroids, adenomyoma | None | None | L.L.Q. pain | Small |
| M. T. 462964 | 62 | S | Fibroma l. ovary | Fibroadenoma 6 by 4 by 3 cm. | - | None | None | Pain, vomiting | Medium |
| L. W. 389061 | 62 | M | Fibroma r. ovary | 2 fibroids, (a) 13 by 10 by 7 cm., (b) 2 cm. | 1 small uterine fibroid | None | None | Acute abdominal glycosuria Abdominal disten- tion | Medium |

GROUP II. THECA-CELL TUMORS

| NAME AND NO. | AGE | STA-TUS | OVARIAN PATH. | DETAILS OF PATH. | OTHER PATH. | ASCITES | HYDRO-THORAX | CHIEF COMPLAINTS | SIZE |
|-----------------|-----|---------|---|---|---|---|--------------|--|--------|
| I. B. 434351 | 58 | M | Theca-cell tumor 7 by 5 by 3 | With small cysts | - | None | None | | Medium |
| B. B. 413016 | 60 | M | Theca-cell tumor 2.5 by 1.5 | Pedunculated Encapsulated | Uterine fibroids Endometrial polyp, chronic appendi- citis | None | None | Attack of "pyeli- tis"; | Small |
| E. D. 426861 | 51 | W | Theca-cell tumor l. ovary 12 by 9 by 6 | Edematous | Adenocarcinoma r. ovary | Small amount of clear serous fluid | None | Lower abdominal pain Weight loss | Medium |
| M. F. 433424 | 52 | S | Theca-cell tumor r. ovary 1.5 cm. diam. | - | Uterine fibroids Serous cyst l. ovary | None | None | L.L.Q. pain | Small |
| A. G. 408827 | 53 | M | Theca-cell tumor l. ovary "large," | Cystic degeneration | Uterine fibroids Edematous Chronic appendi- citis | Serosanguineous fluid, small amount | None | Weight loss Weakness Slight jaundice | Medium |
| F. G. 429914 | 58 | M | Theca-cell tumor l. ovary 17 by 15 by 10 | 17 by 15 by 10 cystic areas | - | No tumor cells Ascites abundant | Right | Dyspnea; leg swelling, en- largement of ab- domen | Large |
| L. H. 429702 | 51 | S | Small theca cell tu- mors pea-sized | - | Uterine fibroids | None | None | Pains in chest | Small |
| B. K. 408858 | 58 | M | R. ovary theca-cell tumor size of small melon | - | - | None | None | Pain in lower ab- domen and back | Medium |
| M. K. 468372 | 29 | S | Theca-cell tumor 15 by 9 cm. | - | Chronic appendi- citis | None | None | | Medium |
| P. K. 484051 | 62 | W | Theca-cell tumor r. ovary 15 by 12 by 8 cm. | Some cystic areas | - | None | None | | Medium |
| Y. L. 482737 | 59 | W | Theca-cell tumors l. ovary 10 by 8 by 4 cm. | Few hemorrhagic areas, in few places moderately softened | - | None | None | Backache | Medium |

In a fourth group, the swelling potential and water attracting power of gelatin was used to simulate the properties of certain abdominal effusions.

In a single but unsuccessful experiment we tried to watch the passage of a contrast medium (hippuran) through the diaphragm under x-ray control.

The results obtained thus far in these experiments were not entirely satisfactory. A moderate accumulation of fluid in the pleural cavity was observed in some of the experiments with saline and in some with serum. The injection of a kaolin suspension into the peritoneal cavity resulted in a blocking effect. The inhibiting influence of gelatin on the absorption of intra-abdominal fluid and its transference into the pleural cavity was also demonstrable. Until recently, we had not succeeded in finding a reliable experimental technique which would artificially reproduce Meigs' syndrome with any degree of regularity. The last experiments made by injecting kaolin and India ink into the pleural cavity first, and carmine solution intraperitoneally four days later revealed carmine-stained fluid in both the pleural and peritoneal cavities three hours after the intraperitoneal injections, but none in either cavity after 16 hours. Large deposits of India ink in the whole mediastinum which was entirely black, spotlike deposits along the vertebra and smaller collections along the intercostal muscles were found. The lateral muscular portion of the diaphragm was not stained with India ink, but the central tendinous portion where it connects with the mediastinum was. These experiments suggest that although the transference of fluid from the abdominal into the pleural cavity is not obstructed from below upward, nevertheless its resorption from the pleural cavity is apparently delayed. That small corpuscular elements like carmine and India ink can be transported from the abdominal into the pleural cavity was uniformly observed by us, corroborating the well-known experiments of other authors mentioned above.

Summary and Conclusions

1. Ascites is not a frequent occurrence in ovarian fibromas if one considers all fibromas including the small ones.

2. Ascites as well as the combination of ascites and hydrothorax (Meigs' syndrome) is also found in theca-cell tumors.

3. The ascitic fluid probably originates from the tumor itself. Geibel's observation on the oozing of fluid from an ovarian fibroma placed in a dry vessel should be verified. The conditions which may bring about a lymph congestion in the tumor should be studied by a thorough examination of the lymph and blood vessels in the tumor tissue, in the pedicle and on its surface.

4. In every case of Meigs' syndrome the specific gravity, the albumin and cell content and the osmotic pressure of the ascitic and pleural effusions should be determined.

5. Further animal experiments are necessary to establish the most favorable conditions for the occurrence of Meigs' syndrome. Experiments with the fluid found in cases of Meigs' syndrome appear to be promising.

6. The anatomic routes by which fluid is transferred from the peritoneal into the pleural cavity are described. Living cells, cell debris or chronic inflammatory changes of the peritoneum or of the pleura may block the connections between these two cavities.

7. The prevalence of right-sided pleural effusions can be explained by anatomic and physiologic conditions, i.e., the better development of the diaphragmatic lymph channels, the higher position of the diaphragmatic dome and the more intensive pumping action of the diaphragm on the right side.

8. A hydrothorax can best come about not only if the ascitic fluid is poor in colloids, and therefore can easily pass the diaphragm, but also if the absorption and deportation of the fluid is not too rapid in the pleura to prevent its accumulation.

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COMPARATIVE ANALYSIS OF DRUGS IN CONTINUOUS CAUDAL ANALGESIA

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FOR almost one hundred years, attempts have been made to relieve the pain of childbirth. During this period, various methods of using analgesic and sedative drugs have been advocated. None of these drug combinations has been entirely satisfactory. The use of continuous caudal analgesia in labor and parturition as reported by Edwards and Hingson⁴ was received with enthusiasm by the medical profession and the lay public.

Several weeks ago, we began using this new type of analgesia. Although it has thus far been impossible to carry out the procedure in a large number of cases, we have made an effort to closely supervise the patients, and to critically analyze the method in regard to its advantages and disadvantages. Particular attention has been given to two analgesic agents.

The history of continuous caudal analgesia has been adequately and completely given in many previous publications.^{1, 4, 5, 10}

The technique that we have used was originally described by Hingson and Edwards involving the use of the malleable needle and intermittent injections of the drug.^{4, 5, 7, 10} We have not used the alternative method devised by Adams and Lundy involving the ureteral catheter.⁸

Two drugs have been used with equal effectiveness, metycaine and pontocaine.* Metycaine was used in 1.5 per cent solution in saline and pontocaine 0.25 per cent in saline and recently 0.1 per cent solution in saline combined with epinephrine in a dilution of one to 200,000. The duration of effective analgesia was of some interest. Metycaine injected in 20 c.c. or 30 c.c. amounts was effective for about thirty to forty-five minutes. Pontocaine 0.25 per cent injected in the same volume produced analgesia for forty-five minutes to one hour, and pontocaine 0.1 per cent plus epinephrine was effective for as long as one and one-half hours.

Among the 100 obstetric patients, there were three patients with pulmonary tuberculosis, three with severe pre-eclampsia, one eclamptic, and one patient with carcinoma of the breast with pelvic metastases.

Advantages

Perhaps the outstanding feature noted in our cases was the small amount of bleeding in the third stage.

*Pontocaine furnished for this study by Winthrop Chemical Company.

There was considerably more blood lost from the episiotomy wound than from the uterus in every case except one. Following one breech delivery, a postpartum hemorrhage occurred. This case offered considerable difficulty in delivery of the aftercoming head, the cord was twice about the infant's neck and undue traction was inadvertently applied to the cord. The placenta delivered rapidly and approximately 500 c.c. of blood followed it.

The remarkably good uterine tone which is maintained throughout the third stage of labor is probably responsible for the apparent diminution in blood loss. The placenta usually separates promptly, and in the majority of cases, is free in the vagina ready for simple expression by the time the operator has cared for the infant. In one case, the placenta was incarcerated by the rapidly contracting uterus and ether vapor anesthesia was necessary to complete the third stage. Coincidental with the excellent uterine tone, there was also apparent shortening of the third stage of labor. A careful analysis of our statistics, however, did not reveal a significant difference in the duration of the third stage between patients delivered under caudal analgesia, and those delivered under inhalation anesthesia.

The second most striking feature of the method is prompt spontaneous respiration in the newborn infant. This assumes particular importance in the delivery of premature infants and in cesarean sections.² We observed no asphyxia neonatorum in any of the babies.

Another feature of caudal analgesia and one which has been much publicized in the lay literature, and to which the method owes its countrywide interest, is the diminution in the intensity of labor pains. In only two of our cases was it necessary to supplement the caudal analgesia with nitrous oxide and oxygen during the delivery itself.

Our observations corroborate the impressions of others that labor should be well established when the analgesia is initiated. In our cases,

TABLE I. CLINICAL MATERIAL

| PROCEDURE | ANALGESIC AGENTS USED | | | TOTAL CASES |
|---|-----------------------|-------------|---|-------------|
| | METY-CAINE | PONTO-CAINE | PONTOCAINE 0.1% WITH EPINEPHRINE 1:200,000 | |
| Low forceps | 20 | 19 | 21 | 60 |
| Spontaneous | 8 | 4 | 1 | 13 |
| Low cervical cesarean section | 2 | 1 | 5 | 8 |
| Breech | 1 | 1 | 1 | 3 |
| Midforceps rotation | 1 | 1 | 2 | 4 |
| Manual rotation | 5 | 1 | 1 | 7 |
| Brow conversion to vertex | 1 | 0 | 0 | 1 |
| Hysterectomy | 2 | 0 | 0 | 2 |
| Salpingo-oophorectomy plus appendectomy | 2 | 0 | 0 | 2 |
| Hysterotomy and sterilization | 0 | 0 | 1 | 1 |
| Thrombophlebitis | 2 | 1 | 3 | 6 |
| Failure to insert needle | 0 | 0 | 0 | 4 |
| Total | 44 | 28 | 35 | 111 |

the cervix was approximately 5 cm. dilated and the interval between pains was five minutes or less at the time the needle was inserted. When these requirements were fulfilled, labor progressed rapidly throughout the first stage. Progress became arrested, however, with complete dilatation due to lack of voluntary expulsive efforts in the second stage, necessitating operative interference in sixty-six per cent of the cases delivered per vaginam. This seemingly disagreeable feature was obviated in two ways; first, by instructing the patient in voluntary "bearing down" efforts and second, by the use of outlet forceps.

With local anesthesia over the perineum, there is complete relaxation of all supporting structures which reduces the incidence of soft part dystocia. The vagina and rectum are readily distensible and dilatation of these organs produces no pain. As a result, complete, thorough and painless rectal examinations can be made. Patients with hemorrhoids may be examined with no discomfort. The cases reported were from the ward service, and their progress in labor was followed by medical students. Many rectal examinations were done by these students in order to familiarize themselves with the progress of the parturient. Caudal analgesia permits thorough examination with no discomfort.

In common with local injection anesthesia and other regional blocks, this procedure eliminates some dangers which are inherent in any inhalation anesthesia. Aspiration pneumonia and atelectasis should not occur. The individual with pulmonary or cardiac disease is more conservatively cared for by this method. Patients may continue to take food and fluids throughout labor and immediately post partum, thereby maintaining fluid and electrolyte balance.

Those patients who have elevated blood pressure resulting from cardiovascular, renal disease or pre-eclampsia, are relieved of the exertion of the second stage of labor. Eclamptic patients may be kept perfectly quiet, and labor pains are less likely to precipitate a convulsion.

There are doubtless many other striking features in favor of this type of analgesia. The above facts have been most apparent in our observations.

Disadvantages

The unfavorable aspects may seem numerous. It is probable that we are, in part, responsible for some of the disadvantages noted. It is also probable that the disagreeable features will largely be eliminated with further knowledge, with improvements in methods, and with the development of new analgesic agents.

The possibility of dural puncture with subsequent injections of massive amounts of the drug into the subarachnoid space is ever present.^{9, 11} If a large volume of the drug is injected intradurally, only heroic methods for maintaining blood pressure and respiration will save the patient. Methods to eliminate this danger have already been devised but no foolproof procedure has as yet been forthcoming.

Closely related to this danger symptomatically is intravenous injection or absorption.³

It is imperative, therefore, that someone relatively familiar with the procedure and capable of intelligent action be in constant attendance throughout active labor in case respiratory arrest or alarming fall in blood pressure should occur. Whereas barbiturates may be given in therapeutic amounts and the care of the patient entrusted to the usual labor-room nurse, one cannot initiate caudal analgesia and leave the patient. In teaching hospitals, where medical students are available under the supervision of trained house officers, the care of the patient offers no difficulty; for the private practitioner this constant observation of the patient is a definite problem.

In regard to the insertion of the needle, certain features are outstanding. In the very obese patients, the sacral hiatus is nearly impossible to identify and insertion is rendered exceedingly difficult. Deformities of the sacrum may even make it impossible. We were unable to properly insert the needle in four patients, including one with spina bifida. Pustules or excoriations about the buttocks, pilonidal cysts or sinuses contraindicate its use. Infection within the canal has been reported.⁶

Caudal analgesia produces loss of desire to void. As a result, it is necessary to aid the patient in this respect by pressure on the bladder above the symphysis in an effort to overcome the internal vesicle sphincter. Even though this is done, frequent catheterizations have to be performed and the possibility of retrograde urinary tract infection is enhanced. We observed three cases of postpartum atony of the bladder requiring active therapy and increasing the hospital stay of the patient. These three individuals received 0.25 per cent pontocaine. No postpartum atony occurred with pontocaine, 0.1 per cent with epinephrine or with metycaine.

Severe nausea and vomiting occurred in two patients who received pontocaine, and in one patient who received metycaine. These symptoms were immediately relieved following delivery of the infant.

The incidence of operative deliveries was increased by the use of continuous caudal analgesia probably as a result of the lack of expulsive efforts of the patient in the second stage.

In breech presentation because of the lack of a firm dilating wedge, and the absence of the "bearing down" sensation, the presenting part remains high and manual aid is necessary very early in the conduct of the second stage.

Finally, it should be pointed out that certain emotionally unstable individuals are exceedingly fearful of childbirth. Those who are in any way mentally unstable are very poor candidates for this type of analgesia.

Conclusions

1. Pontocaine 0.1 per cent with epinephrine 1 to 200,000 is a safe and satisfactory caudal analgesic agent.

2. Pontocaine 0.25 per cent and pontocaine 0.1 per cent without epinephrine have been unsatisfactory.

3. Caudal analgesia has great possibilities for use in obstetrics and in surgery of the pelvis. It is possible to relieve pains of labor during the first stage, and to produce anesthesia for delivery.

4. The baby's respiration is established immediately and no resuscitation is necessary.

5. The method is one to be used only by persons familiar with local and regional anesthesia, and aware of the dangers involved.

6. Caudal analgesia is unsatisfactory in patients with breech presentations.

7. Since the mechanism of labor is altered with the use of continuous caudal analgesia, no one should attempt to use this method unless he is familiar with the techniques of rotation of the fetal head, and the use of the obstetric forceps.

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PLACENTAL INFARCTION AS A DIAGNOSTIC CRITERION OF MATERNAL TOXEMIA

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SINCE clinical experience has repeatedly demonstrated that the manifestations of late toxemia of pregnancy can be quickly relieved by emptying the uterus, it has been reasonable to suspect a connection between the placenta and toxemia. To this end, many have searched for placental lesions having a high degree of correlation with maternal toxemia. The lesions that have attracted the most attention have been the so-called "infarcts," a term used to include a variety of lesions. The causal relationship between placental infarction and maternal toxemia has not been generally accepted even though they are frequently associated. However, Bartholomew and co-workers¹⁻⁴ have stated that a high degree of correlation between certain acute infarcts and toxemia does exist, and they have presented evidence that these lesions have etiologic significance.

The work† presented here is the result of the gross examination of 640 consecutive placentas in an unsuccessful attempt to find lesions characteristic of toxemia.

Siddal and Hartman¹⁰ in 1926, described four types of infarcts found in 67.7 per cent of 700 consecutive placentas which they studied. All were composed largely of degenerated villi and elements from the maternal blood. Their first three types resembled intravascular thrombosis and depended "upon stasis of the maternal blood flow in the intervillous placental space and the existence of areas denuded in some way of their anti-coagulative syncytial epithelium."

Their Type 1 infarct was described as a poorly defined or irregular, pearl-gray formation varying in size from microscopic areas to those several centimeters in width. They were not striated, and often had a mottled appearance near the outside due to the partial inclusion of small areas of normal placental tissue. Microscopically, the central portions of advanced infarcts had a solid structure composed of degenerated shadows of villi surrounded by old fibrin. Near the periphery, broad projections of fibrin extended to nearly normal villi.

Their Type 2 infarct was located usually toward the center of the cotyledon and varied in color from red, brown, or almost black to pink or brick-colored. It measured a few millimeters to several centimeters in diameter. Frequently, it was sur-

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rounded by a pale pseudocapsule. Some were striated. Microscopic examination revealed the lesion to be composed of lamellae of fibrin and coagulated blood. They were at times found lying against Type 1 or Type 4 infarcts, but otherwise showed practically no involvement of the villi.

Their Type 3 infarct resembled Type 2, but was less dark in color due to the absence of blood pigment. Intermediate forms between Type 2 and Type 3 were seen.

Their Type 4 infarct was described as being usually near the margin of the placenta, and varying from a few millimeters in diameter to the involvement of whole cotyledons. The older forms of this type were a uniform dull white or light yellow with edges contrasting sharply with the surrounding placental tissue. The younger forms were pink, or even dark reddish-brown and were usually mottled. Microscopic sections revealed these lesions "to be composed of closely packed villi, usually, a thin layer of fibrin between." A characteristic feature was that all the villi had reached about the same degree of degeneration. In recent lesions, the syncytium and intravillous blood appeared normal with only the stroma showing degenerative changes. In older lesions, the intravillous erythrocytes were faded and disintegrated, the syncytium eventually degenerating while the stroma had lost nearly all evidence of its cellular structure.

Siddal and Hartman stated their Type 4 lesion "probably represents a simultaneous involvement of all the branches of a stem villus due to disturbance in the fetal-placental circulation." They found all types of infarction to be more frequent in placentas from cases of toxemia. In the forty-five placentas from cases of toxemia, 86.7 per cent had infarction of some type. According to types, 17.8 per cent had Type 1, 31.1 per cent had Type 2, 37.8 per cent had Type 3, while 42.2 per cent had Type 4 infarcts.

In 1932, Bartholomew and Kracke³ wrote that eclampsia resulted from absorption into the maternal blood of the split products of placental protein from an acutely infarcted area. The infarcts they considered significant apparently belonged to Siddal and Hartman's Type 4. In 1936, Bartholomew and Kracke⁴ stated that hypercholesteremia of pregnancy was probably the fundamental basis of toxemia since its excessive storage in the placental arteries predisposed to infarction. In 1938, Bartholomew¹ stated: "Toxemia of pregnancy is associated with definite types of acute infarction of the placenta. In examining 'unknown' placentas, it is possible to diagnose pre-eclampsia, eclampsia, and abruptio placentae in 90 per cent of the cases." This statement was based on Bartholomew and Colvin's² work in which they examined 100 placentas grossly as unknowns from both toxemic and normal cases. They also said it was possible to predict the type of infarcts that would be found in the placenta from a knowledge of the clinical history of the pregnancy. Their 100 cases were selected and were not from consecutive deliveries. Fifty of the placentas were from normal cases, twenty-four were from cases of mild to moderate toxemia, eight were from cases of pre-eclampsia, ten were from cases of eclampsia, while two were from cases of abruptio placentae. They classified infarcts as A, B, C, D, and E in the order of increasing rapidity of in-

farcion, as well as in the order of increasing toxicity. Their descriptions are as follows (Bartholomew¹):

"If infarcion occurs rapidly, the affected placental tissue appears as one or more round or oval areas from one to several centimeters in diameter which are sharply demarcated from the surrounding normal placental tissue by the *color*, which is a dark, purple-black color. These areas correspond to the distribution of the obstructed vessel. The consistency is still spongy and soft as in normal placental tissue. When the strip is held toward the light, the infarcted area preserves a granular appearing surface. When the strip is bent, the infarcted area bends as easily as the normal tissue. There may be a soft or firm clot within, or adjacent to the area. This type of infarct is designated as the early E infarct. Clinically, the acute type of infarcion is associated with the more acute, fulminating, pre-eclamptic, eclamptic, or abruptio type of toxemia, and there is a direct relation between the amount of tissue involved and the severity of the toxemia. It is usually found when the patient progresses from a normal state to pre-eclampsia, eclampsia, or abruptio placentae within a week or ten days.

"If infarcion is slightly older or less acute (late E infarct), the lesion is still dark or purple-black, but has changed from a spongy to a more compact, firm area, sharply demarcated from the surrounding lighter spongy tissue. It is firmer to palpation, and when the strip is held toward the light, the surface of the lesion appears marble-like and shiny. When the strip is bent, the infarcted area either cracks sharply or holds together and does not bend with the rest of the strip. Clinically, the toxemia is almost, if not quite, as fulminating as that associated with the early E infarct. . . . If infarcion is still less acute or of longer duration, corresponding to a clinical course of from two to three weeks, the infarcts vary from a faint brown (early D) to a definite brown (late D) and are sharply demarcated, firm, compact, smooth, and shiny and hold together when the strip is bent. Grossly, the more rapid the infarcion, the less conspicuous the lesion, the less firm the consistency, the darker the color, and the greater the toxicity. The range in color, due to change in the hemoglobin, is from very dark purple-black in infarct E to brown in D, to brown-yellow in C, to yellow-white in B, and to white in A. The size and number of the infarcts bear a definite relation to the severity of the toxemia. Failure to appreciate the relationship between placental infarcts and toxemia of pregnancy has been due to improper preparation and examination of the placenta and lack of familiarity with the more acute types of placental infarcts."

Schumann⁹ wrote that no distinct connection between toxemia and placental infarcion could be established, and, remarked that for years he had pointed out to his interns and students the absence of marked infarcion in placentas from severe cases of eclampsia. Furthermore, he noted cases having striking areas of placental infarcion with uneventful pregnancies.

Harer⁶ in 1936, stated that the placental changes found in late toxemia were identical with but occurred more frequently and were more extensive than those found in clinically normal cases. He regarded maternal toxemia as an additional source of injury to an organ already undergoing the pathologic changes incidental to senility.

Tenney¹¹ in 1936, reported that moderate syncytial degeneration was present in mature normal placentas. In placentas from cases of severe toxemia or eclampsia, the syncytial degeneration was sufficiently

marked as to be of diagnostic value. In 1940, Tenney and Parker¹² stated that toxemia could be accurately judged by placental histopathology.

Hunt, Patterson and Nicodemus⁸ in 1940, stated "early in a study of this kind one may become discouraged because grossly the placenta may show very little. This is often true even after fixation." However, after studying 180 placentas microscopically and adding the findings to those of the gross examination, they believed placental lesions of vascular origin were "primary" in the production of late toxemia.

It is our opinion that no conclusions regarding the presence or absence of maternal toxemia may be drawn from gross examination of the placenta, even though it has been well fixed. We arrived at this conclusion after gross examination of 640 placentas and studying the clinical record of each case.

After we had examined several hundred placentas, we were impressed by the fact that the cut section in some instances was light brown in color, while in others, it was a dark, purplish-brown, the difference in color being due to the amount of blood contained in the specimen. The dark placentas represented congestion. We were thus able to divide our specimens into three groups depending on the appearance of the cut section after fixation, i.e., (1) light, (2) medium, (3) dark. The practical importance of investigating the causes of the different colors was that Bartholomew and Colvin apparently identified their E infarcts chiefly by their color. In the majority of cases, their anatomic diagnosis of toxemia was made on the identification of the E and D infarcts. Obviously the E and even the D infarcts, would be difficult to see in a dark congested placenta.

In 1936, Harer⁶ found congestion in 25 per cent of his series and discussed the cause and prevention of the condition. He stated "the majority of these cases are caused by interference with the maternal blood supply to the placenta and are due to a reduction in the area of the placental site." He thought that in most cases congestion occurred late in labor, or even after birth of the child and was apparently without effect on the mother or child. Among the mechanisms he thought might produce this condition was that the contracting uterus might compress the thinner-walled uterine veins before the thicker-walled arteries could be completely shut off. In forty-three cases he managed the third stage of labor as follows: The umbilical cord was cut and the placental end allowed to drain. No oxytocics were administered, and the uterus was not touched until definite evidence of placental separation was observed. In none of these cases did he find an instance of passive congestion.

In a small series of twenty-five cases, we found that allowing the umbilical cord to drain prevented the occurrence of placental congestion.

Materials and Methods

Six hundred and forty placentas obtained from women delivered in the hospital provided the material for this study. Within one to two

hours after delivery, the placentas were placed in 4 per cent formaldehyde solution and sent to the laboratory where the membranes were removed and excess blood wiped off. The specimens were fixed in 10 per cent formaldehyde solution for four to six weeks, and then cut into strips about one centimeter wide. The presence and extent of certain kinds of infarcts were observed, and on this basis a diagnosis of "toxemia," "questionable toxemia" or "no toxemia" was made. The diagnosis was then checked at once with the clinical record. Special attempts were made to identify the acute E infarct of Bartholomew.

A persistent hypertension of at least 140/100 which fell to within normal limits after delivery, albuminuria and edema all in the last trimester of pregnancy constituted our clinical criteria of toxemia. Forty-two or 6.5 per cent of the 640 cases were toxemias, and five or about 0.8 per cent were eclampsias. Blood pressure determinations were routinely made in all cases during labor until delivery. We did not encounter any proved cases of nephritis.

Siddal and Hartman's Type 1 and Type 4 infarcts both involve necrosis of placental villi whereas their Type 2 and Type 3 do not. We therefore selected the former two types of infarcts as our anatomic basis of diagnosing toxemia. We also attempted to use Bartholomew and Colvin's E infarct as a criterion for the anatomic diagnosis of toxemia. Areas of infarction less than one centimeter in diameter were arbitrarily disregarded except in the rather infrequent placentas containing a great many such small lesions.

Results

We diagnosed toxemia correctly in only eight or (19 per cent) of the forty-two placentas from cases of toxemia. The diagnosis was questionable in seven (16 per cent), while twenty-seven (64 per cent) of these forty-two placentas were passed by us as showing no more infarction than our normal placentas. Thirteen (2 per cent) of our 598 placentas from normal pregnancies revealed sufficient infarction to cause us to wrongly diagnose toxemia. Of the five placentas from cases of eclampsia, three were diagnosed as "questionable toxemia," while two were passed as normal.

From these data, it is evident that we could not recognize lesions characteristic of maternal toxemia by gross examination of the placenta.

We failed to identify to our complete satisfaction the acute kind of lesion which Bartholomew and Colvin² described in their placentas from cases of toxemia.

Placental Congestion

We have pointed out the desirability of having placentas free from congestion since congestion may mask the acute infarcts described by Bartholomew and Colvin.² Acting on Harer's⁶ belief that congestion

depended on the manner in which the third stage of labor was managed, we studied 125 placentas from two standpoints.

We determined first, the effect of administering pituitrin at the end of the second stage of labor upon the incidence of congestion of the placenta. One hundred cases were studied of which fifty-four received pituitrin at the end of the second stage, while the remaining forty-six received no pituitrin during labor. The placentas were classified as "light," "medium," or "dark" depending on the appearance of the cut section. Of the forty-six placentas from cases receiving no pituitrin, fifteen (33 per cent) were "light," seventeen (37 per cent) were "medium," while fourteen (30 per cent) were "dark." Of the fifty-four placentas from cases receiving pituitrin, twenty-two (40 per cent) were "light," twenty (38 per cent) were "medium," while twelve (22 per cent) were "dark." These results are summarized in Table I. It is evident that the giving or withholding of pituitrin had no significant effect on the incidence of congestion of the placenta.

TABLE I. THE EFFECT ON THE COLOR OF THE PLACENTA OF GIVING PITUITRIN OR DRAINING THE UMBILICAL CORD

| | PITUITRIN GIVEN | NO PITUITRIN | UNBILICAL CORD DRAINED |
|------------------|--------------------|-----------------|---------------------------|
| | 54 Cases | 46 Cases | 25 Cases |
| Light placentas | 22 | 15 | 21 |
| Medium placentas | 20 | 17 | 4 |
| Dark placentas | 12 | 14 | 0 |

We next determined the effect of allowing the umbilical cord to drain free of blood as soon as possible after birth of the baby. While we were able to secure only twenty-five cases in which this was done, the results were striking. Twenty-one (84 per cent) were "light," four (16 per cent) were "medium," while none was "dark." These results are also summarized in Table I. It is suggested that allowing the umbilical cord to drain may be of value in avoiding or lessening passive congestion of the placenta.

Comment

In a study of this kind, we are convinced of the necessity of using unselected cases. In our series, the incidence of placentas from cases of toxemia was only 6.5 per cent. Furthermore, the abnormal ones were not regularly encountered. We would examine at times as many as thirty placentas from clinically normal cases before encountering one from a case of toxemia. If one were to examine a selected series of placentas in which half were from cases of toxemia, the possibility of picking out such placentas would be greatly increased by chance alone as compared to a group of consecutive unselected cases.

We cannot explain our failure to find the acute infarcts described by Bartholomew and Colvin² in the placentas from cases of toxemia.

Although placental congestion might obscure this lesion, it is unlikely that congestion occurred in all our placentas from cases of toxemia. While twenty-five cases are not enough on which to base a conclusion, we suggest that the umbilical cord be drained to prevent masking of a lesion by congestion.

Haselhorst and Allmeling⁷ found that the average amount of blood in the placental vessels of 120 infants was 104 cubic centimeters. They showed that 51 per cent of this flowed into the infant from the placenta in the first minute after delivery, 79 per cent reached the child in the first five minutes, and 91 per cent in the first ten minutes. DeMarsh, Alt and Windle⁸ collected and measured the blood in ten placentas at the end of pulsations (about three minutes after birth), and the amounts averaged 62.4 cubic centimeters. They stated: "A delay on the part of the obstetrician in clamping the cord, not only until pulsations cease but also until the placenta has separated from the uterus, will give the newborn infant the quota of blood that naturally belongs to him." From these observations we suspect that the placenta will be congested in cases where the cord is clamped immediately. Congestion of the placenta may be avoided by delay in clamping the cord as well as by allowing it to drain.

It was of interest to discover the nearly identical incidence of toxemia and eclampsia in Siddal and Hartman's¹⁰ series, and in the series we are reporting. Both were consecutive series of cases delivered in the hospital. Their series had forty-five cases of toxemia (6.4 per cent) of the total 700 cases. Our series had forty-two cases of toxemia (6.5 per cent) of the total 640 cases. In each series there were five cases of eclampsia.

Summary and Conclusions

The placentas from 640 consecutive deliveries were fixed in 10 per cent formaldehyde solution for four to six weeks, and then examined grossly for certain infarcts involving necrosis of the villi. Forty-two placentas were from patients with a definite clinical picture of toxemia.

Examining them all as unknowns, only eight of these forty-two placentas from cases of toxemia had such infarcts extensive enough to distinguish them from placentas of nontoxemia cases. Thirteen of the 598 placentas from patients with normal pregnancies showed infarcts like the eight from cases of toxemia.

We were unable to satisfy ourselves that we could recognize the acute type of infarct described by Bartholomew and co-workers as being associated with toxemia.

In twenty-five placentas, the cord was drained. There were no instances of congestion when this was done. Administration of pituitrin at the end of the second stage of labor did not affect the incidence of congestion. Congestion might obscure some placental infarcts.

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THE APPLICATION OF THE BRAXTON HICKS VERSION IN MODERN OBSTETRICS

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IN MEDICINE, certain procedures have frequently been lost with the passing of years, and on occasion, their value has not been sufficiently appreciated. The operation of bipolar version as first advocated by J. Braxton Hicks¹ appears to fall into such a category. With the advent of anesthesia and asepsis, it is possible to offer certain modifications to the original operation. Furthermore, improved techniques have been developed since the advent of the original monograph. It is, therefore, appropriate to reconsider and attempt to re-evaluate this operation in accordance with the progress of obstetrics.

In many of our present textbooks on obstetrics, we find this operation limited, for the most part, to the treatment of placenta previa. Irving,² in advocating the operation, described the technique, emphasized the technical difficulties encountered, and reported the results in a series of patients composed primarily of individuals who developed severe ante-partum bleeding in the last trimester of pregnancy. Most of the cases were patients with placenta previa and a smaller group with premature separation of the normally implanted placenta. The procedure was used when the babies were nonviable, extremely premature, or dead at the time of operation. He suggested that the operation was applicable to other groups of cases, particularly to patients with severe preconvulsive or convulsive toxemia where the babies were very premature or the operation of abdominal hysterotomy was too great an operative risk for the mother.

In his original monograph "On Combined External and Internal Version," published in 1864, J. Braxton Hicks presented twenty-four cases treated by this operation which now bears his name. About 50 per cent of the cases in his report were patients with placenta previa. Ten of the remaining cases were actually individuals with cephalopelvic disproportion, with over half of the infants presenting in a transverse position. There was one patient who had eclampsia, and two cases in which the cord had prolapsed. Naturally, with the advent of cesarean section since that time, many of the conditions he reported would have been treated by this surgical procedure. Hicks was conscious of two principles which must be adhered to in order to facilitate the successful performance of his operation, namely:

1. The desirability of intact membranes, or, if not intact, the rupture of the membranes should have occurred only recently.

2. Once the baby is turned, and a foot is brought through the partially dilated cervical os, delivery should depend only upon the natural forces of labor.

This report is concerned with further experience with this operation. We believe that its usefulness can be applied to patients with pregnancy toxemia, abnormal presentation of the fetus, malformation of the fetus, as well as to patients with late antepartum vaginal hemorrhage. Experience has taught us that certain modifications, added to the operation, simplify the technique.

Antepartum Bleeding in the Last Half of Pregnancy

It is the general policy of this clinic to deliver patients with placenta previa (maginal and partial) by the vaginal route, if the baby has little chance of survival.³ Although, occasionally, we have successfully delivered patients with central previa by the vaginal route, we do not recommend this treatment as a routine procedure. Many of these cases were treated directly with bipolar version, while others were first treated with a Voorhees bag if the cervical os was one finger or less dilated.

When the latter procedure is necessary, the question arises whether this form of cervical tamponade is most effective, if the bag is placed within or outside the amniotic sac. There are certain advantages to either method. Those who advocate the intraovular insertion of the bag believe this method is necessary for the proper control of the bleeding. One must concede that the bleeding is better controlled if such an insertion can be accomplished. However, this is not always possible, for, not infrequently, the placenta detaches itself from the uterus by the force of the clamp as it attempts to burrow through the placenta in order to insert the bag within the ovum. This accident may initiate such a degree of immediate hemorrhage that, often, the operator will have to be satisfied with an extraovular insertion. Although the placenta is thus separated from its site, immediate inflation of the bag will cover the maternal sinusoids with subsequent thrombosis. Therefore, only a modicum of hemorrhage can occur. However, as labor progresses and the cervix becomes further dilated, the bag will not rest firmly against the lower segment and consequent bleeding may ensue. Hence, a good sense of timing is necessary in removing the bag and performing the bipolar version, if one is to maintain minimum blood loss.

In addition, two other advantages can be considered when the insertion of the bag is extraovular. First, if the membranes are kept intact, they will form an important barrier against intraovular infection, and, second, the preserved fluid of the intact amniotic sac will allow the uterus to be relaxed and moist for performing the bipolar version.

Pregnancy Toxemias

The toxemias of pregnancy are a disease occurring chiefly in the latter half of gestation. Frequently, termination of the pregnancy is

mandatory if one is to serve the best interests of the mother. It has been generally accepted that artificial termination of pregnancy, pelvically, from the twentieth through the thirty-fifth week, can be unsatisfactory and often hazardous. The nonirritability of the uterus at this time does not augur well for the production of effective labor by simple rupture of the membranes. Also, noneffacement and lack of dilatation of the cervix present impediments to effectual labor. The latent period following artificial rupture of the membranes, in such cases, may consume days or even weeks before labor ensues, thereby augmenting the risk to patients with severe pregnancy toxemia in at least two ways: (1) the increase in the severity of the disease before the uterus is successfully emptied of the products of conception, and (2) the danger of severe intrapartum and postpartum uterine infections.

The following forms of treatment have been advocated for the termination of pregnancy during this period:

1. *Bougies*.—The same criticism relative to the simple rupture of the membranes appears valid, in addition to the danger of traumatic separation of the placenta.

2. *Vaginal Hysterotomy*.—Certainly, the trauma and blood loss are too unpredictable for one to recommend the operation as a routine procedure. This is especially true if the patient is a primipara where technical difficulties associated with inadequate operative exposure may be encountered. The application of this operation should be restricted, for the most part, to multiparous patients in the middle trimester of pregnancy.

3. *Abdominal Hysterotomy*.—This appears to be an extremely radical policy, particularly in patients with severe pregnancy toxemia. Furthermore, the jeopardy to such patients for future childbearing, with the presence of a uterine scar, is certainly increased.

4. *A Voorhees Bag*.—This has always been considered a moderately effective means of inducing labor. However, it may fail. In order to insure against such failure, we recommend:

5. *Bipolar Version (Braxton Hicks)*.—This operation, with or without the use of the bag, is advised:

(a) In cases with severe pre-eclampsia where the baby has a small chance of survival because of prematurity and especially if the patient's toxemic state is rapidly progressing toward eclampsia. Cesarean section is restricted to patients in this group when the baby is not premature and the cervix is not favorable for successful induction of labor by artificial rupture of the membranes, or to cases with definite cephalopelvic disproportion.

(b) In patients with eclampsia, regardless of the maturity and condition of the baby if the cervix is not favorable for induction by artificial rupture of the membranes. The increased peril of an abdominal procedure should be avoided, if possible, even if it means increased infant

mortality. A section is performed only rarely on the eclamptic patient who has definite cephalopelvic disproportion and whose condition is not critical.

It is the routine of this clinic to treat patients in these two groups medically for twenty-four to seventy-two hours until their pulse and blood pressure become stabilized, and their general condition is improved. After such a regimen, further delay is not advisable and evacuation of the uterine contents should be started.

The patient is then anesthetized and prepared for a sterile vaginal examination. The proper instruments should be in readiness for the insertion of the Voorhees bag. If, happily, the cervix is found to be dilated one and one-half fingers or more, immediate Braxton Hicks version can be performed in the classical manner. Frequently, a sponge forceps is used to gently ease the baby's foot through the cervix. This will not place any undue tension on the cervix, in contrast to the possible trauma engendered by bringing simultaneously through the cervix the fetal foot and the two fingers grasping it. When bleeding is not a problem, a weight on the infant's foot is unnecessary. The case, then, is deferred to nature.

On the other hand, if the cervix is not found to be effaced or dilated, a small Voorhees bag is inserted. Occasionally, it will be necessary to dilate the cervix gently with a dilator to permit the introduction of the bag. We have found that a small bag, a No. 2, is more effective than a large one. After the bag is properly inflated, the stem is tied and left within the vagina to prevent contamination. A sulfanilamide gauze strip is packed lightly into the vagina.

The bag is allowed to remain in place for twenty-four to thirty-six hours. During that time indefinite uterine contractions are observed. Although labor often is desultory, the cervix does become effaced and at least one and one-half to two fingers dilated. The bag is then removed. The membranes are artificially ruptured. If the breech is presenting, a foot is brought through the cervix. If the vertex is presenting, a bipolar version is performed, and the case is left to the natural birth processes. Once a foot is brought through the cervix, effective contractions quickly follow.

At this time, we must emphasize two additions to the technique which, we believe, will lend to the ease of performance:

First, great care is taken *not* to rupture the membranes when the bag is being introduced.

Second, the fetus is converted into a breech presentation by an external podalic version. Usually, this maneuver is executed following the insertion of the bag while the patient is still under anesthesia. The upward displacement (by the bag) of the vertex facilitates the external version. When the bag is removed, the fetus will be presenting by the breech. Simple rupture of the membranes usually will allow the infant's feet to drop near the internal os and a foot can be easily extracted.

Malpositions

In his original monograph, Braxton Hicks realized the value of his bipolar version in correcting, partially, the malposition of the fetus if it presented in the transverse position. Unfortunately, marked pelvic contractures were included in many of his cases, and although the mothers were safely delivered, the babies were lost. Certainly, a cesarean section would have been the treatment of choice in most of those patients.

Although it cannot be stated that bipolar version is the policy pursued in this clinic in treating the patients with transverse positions, we believe that it does have a limited use in selected cases. Teel, in this clinic, advocated its use in women who had borne many babies, in whom the transverse position of the fetus appeared to occur only because of marked relaxation of the patient's abdominal wall and uterus. Certainly, the operation is of little value in primiparous women at term when the cephalopelvic relationship cannot always be determined with accuracy. In these cases, a high fetal mortality will attend any type of pelvic procedure.

It is interesting that, until two or three decades ago, bipolar version was used many times for the correction of this type of abnormal presentation. Later, it was discredited because of the high fetal mortality which attended the operation. Undoubtedly, such a high fetal mortality was a result of the fact that many times the operator did not allow the patient to continue in labor, once a foot was brought down. Rather, immediate extraction was performed in the presence of the partially dilated cervix. This resulted in the usual disastrous consequences to both mother and child.

Certain aspects pertinent to the use of bipolar version arise in these cases. If the patient is observed in early labor, external cephalic version may be attempted with fair success. If this fails, the question always arises whether it is better to insert a Voorhees bag, with the hope of keeping the membranes intact rather than allow the membranes to rupture prematurely during labor, with a subsequent dry uterus. Version, in such circumstances, often imperils both the mother and infant. Therefore, there is considerable merit in preserving the membranes by mechanical means, if possible, at least until two to three fingers' dilatation of the cervix is obtained. The bag then can be removed, a bipolar version performed, and the case left to the natural forces of labor. Likewise, if the membranes rupture spontaneously, immediate vaginal examination should be performed. If the cervix is sufficiently dilated, it would seem wiser to perform bipolar version at this time rather than later, when the uterus becomes dry and tightly contracted about the fetus.

Undoubtedly, the question of increased fetal mortality will be raised. This objection is more theoretical than real. Bipolar version, in these

cases, does not interfere with the fetal circulation, as in placenta previa. Following the version, the fetus actually assumes only the mortality of a single footling breech presentation. Certainly, one would not be concerned if a patient began labor with this type of presentation. When the cervix becomes dilated, routine breech extraction can be performed.

Malformations

In malformations of the fetus, complications may arise in the actual mechanism of labor and delivery. This is particularly true in cases of hydrocephalic or anencephalic monsters. Spontaneous rupture of the membranes, especially when hydramnios is present, may result in separation of the normally implanted placenta because of the sudden release of intrauterine pressure. Furthermore, complete dilatation of the cervix will not occur because of the lack of conformity of the infant's presenting part to the lower uterine segment.

We can prevent spontaneous rupture of the membranes and possible subsequent separation of the placenta by the insertion of a small Voorhees bag. If the case is one of hydrocephalus, the bag can be removed when the cervix is one-third or more dilated. The membranes can be ruptured and the liquor amnii allowed to escape slowly. Thus, with a moist uterus, the hydrocephalic head can be perforated and a Braxton Hicks version performed. One only has to recall the unsatisfactory operation of craniotomy on such friable skulls to appreciate the value of this procedure. Likewise, confidence of a prompt and safe delivery of a patient with an anencephalic monster can be assured by the Braxton Hicks operation.

Postpartum hemorrhage due to uterine atony is always an increased hazard in these cases. Overdistention of the uterus is the potential causative factor. Normal uterine tone is best regained by slow decompression of the uterus rather than by sudden release of the intrauterine pressure. This can be effected by the restrained release of the liquor amnii, achieved by the "stopper effect" of a small Voorhees bag. Gradual extrusion of the fetus following bipolar version further enhances this slow decompression.

Indications

One hundred and ten Braxton Hicks versions were done at the Boston Lying-in Hospital between 1930 and 1942, inclusive. The indications, morbidity, and maternal mortality are tabulated (Table I). Twenty-two patients were febrile following delivery, establishing a morbidity rate of 20.0 per cent. The two maternal deaths result in a mortality rate of 1.8 per cent for the series.

Antepartum Bleeding.—There were fifty-one cases of antepartum bleeding treated by this method. The results are listed in Table II.

The degree of placenta previa was not a contraindication for this method of treatment when the infant had little chance of survival. The

TABLE I. INDICATIONS FOR TERMINATION OF PREGNANCY AND RESULTS

| INDICATION | NUMBER OF CASES | FEBRILE PUERPERIUM | MATERNAL DEATHS |
|-------------------------------------|-----------------|--------------------|-----------------|
| Eclampsia | 7 | 2 | 1 |
| Severe pre-eclampsia | 28 | 3 | 1 |
| Placenta previa (all types) | 35 | 7 | 0 |
| Premature separation of placenta | 16 | 5 | 0 |
| Transverse presentations | 10 | 2 | 0 |
| Hydramnios with fetal abnormalities | 8 | 2 | 0 |
| Chronic nephritis | 4 | 0 | 0 |
| Miscellaneous | 2 | 1 | 0 |
| Total | 110 | 22 (20%) | 2 (1.8%) |

TABLE II. ANTEPARTUM BLEEDING CASES

| | NUMBER OF CASES | PRIMI- PARAS | MULTI- PARAS | BAG | TIME IN HOURS BETWEEN VERSION AND DELIVERY | MATERNAL | |
|----------------------------------|-----------------|-----------------|-----------------|-----|--|-------------------------|--------|
| | | | | | | FEBRILE PUER- PERIUM | DEATHS |
| Placenta previa (all types) | 35 | 5 | 30 | 7 | 4.5 | 7 | 0 |
| Premature separation of placenta | 16 | 3 | 13 | 2 | 7.5 | 5 | 0 |
| Total | 51 | 8 (15.7%) | 43 (84.3%) | 9 | 6.4 | 12 | 0 |

results obtained in these cases are exhibited in Table III. Since most of the patients were multiparas, their cervixes were sufficiently dilated at the time of examination to allow for immediate version. It was necessary to use the bag only in nine cases. The bag was placed extra-ovularly in every case with satisfactory results.

TABLE III. BRAXTON HICKS, FOR COMPLETE PLACENTA PREVIA

| NUMBER OF CASES | PARITY | WEEKS PREG- NANT | BAG | TIME BETWEEN VERSION AND DELIVERY | | FEBRILE PUER- PERIUM | DEATHS | OUTCOME OF INFANT |
|-----------------|--------|---------------------|-------|-----------------------------------|--------------|-------------------------|--------|-------------------|
| | | | | HOURS | MIN- UTES | | | |
| 1 | ii | 20 | No. 3 | 23 | 0 | 0 | 0 | Nonviable |
| 2 | vi | 16 | 0 | 3 | 0 | 0 | 0 | Nonviable |
| 3 | ii | 36 | 0 | 0 | 30 | 0 | 0 | Stillborn |
| 4 | x | 27 | 0 | 3 | 0 | 0 | 0 | Nonviable |
| 5 | iv | 26 | 0 | 16 | 0 | 1 | 0 | Nonviable |
| 6 | iii | 34 | No. 4 | 7 | 0 | 0 | 0 | Stillborn |
| 7 | ix | 31 | 0 | 3 | 30 | 1 | 0 | Stillborn |
| 8 | i | 31 | 0 | 3 | 30 | 0 | 0 | Stillborn |

Accouchement forcé should never be employed when the Braxton Hicks version is performed because there is too much danger of rupturing the lower uterine segment. This accident occurred once in this series. The occasion for therapeutic interruption was persistent vaginal bleeding in a 36-year-old para viii, 28 weeks pregnant. Since the cervix was only one finger dilated, the Goodell dilator was used and a foot was

brought down. Subsequently, the patient went into shock. Four blood transfusions were given, and immediately after pelvic delivery, a supra-vaginal hysterectomy was performed. A rupture of the left lower uterine segment was found. It is quite obvious that the insertion of a small bag, with subsequent bipolar version, would have prevented this serious accident.

Bipolar version was performed in sixteen cases of severe toxic separation of the placenta, without any deaths. However, we believe that this operation adds little to the successful termination of pregnancy for this grave obstetrical complication. Artificial rupture of the membranes, with the application of a Spanish windlass type of abdominal binder, is all that is necessary to properly control the bleeding. This can be done without the administration of an anesthetic. Because most of these patients are nearer term than the patients with placenta previa, labor usually begins soon after this procedure. Attempting to hasten such a process by performing a Braxton Hicks version, which necessitates the administration of a deep inhalation anesthetic, further jeopardizes the recovery of a patient who already is suffering from some degree of shock.

Toxemias of Pregnancy.—The results in cases of severe pre-eclampsia and eclampsia are listed in Tables IV and V, respectively. The bag was used in over 75 per cent of the cases. This was necessary because the patient was either late in the middle trimester, or in the early part of the last trimester of pregnancy. Hence, the cervix was not dilated sufficiently to perform an immediate Braxton Hicks version. Simple rupture of membranes in this group would not have insured labor or delivery within a reasonable time. The average time from bipolar version to delivery for this group was 8½ hours.

TABLE IV. HYPERTENSION AND/OR ALBUMINURIA OF PREGNANCY, SEVERE PRE-ECLAMPSIA

| | NUMBER OF CASES | AVERAGE WEEKS PREGNANT | ALBUMIN | BLOOD PRESSURE | | DILATATION OF CERVIX IN FINGERS | BAG | AVERAGE TIME IN HOURS BETWEEN VERSION AND DELIVERY | FETAL PUERPERIUM | DEATHS |
|-----------|-----------------|---------------------------|---------|-------------------|------------|------------------------------------|-----|--|---------------------|--------|
| | | | | SYSTOLIC | DIASTOLIC | | | | | |
| Primipara | 10 | 28.0 | 3 to 4+ | 160 240 | 110 100 | 0 to 1 | 10 | 11.5 | 0 | 0 |
| Multipara | 18 | 28.5 | 3 to 4+ | 150 228 | 100 118 | 1 | 11 | 10.5 | 2 | 1 |
| Total | 28 | 28.3 | 3 to 4+ | 150 240 | 100 118 | -- | 21 | 10.9 | 2 | 1 |

There were two maternal deaths in this entire series. Both occurred in the toxemic group. One patient was delivered by the use of a bag

and Braxton Hicks version and succumbed to eclampsia on the third postpartum day. She was in deep coma throughout her hospital course. Even if pregnancy had been terminated more promptly by cesarean section, it is doubtful that she would have survived. The second death occurred in a patient with severe pre-eclampsia who died from a large pulmonary embolus on the tenth postpartum day. This was verified at necropsy.

TABLE V. HYPERTENSION AND/OR ALBUMINURIA OF PREGNANCY ECLAMPSIA

| NUMBER OF CASES | WEEKS PREGNANT | PARITY | MAXIMUM BLOOD PRESSURE | MAXIMUM ALBUMIN | DILATATION OF CERVIX IN FINGERS | BAG | TIME BETWEEN VERSION AND DELIVERY | | FEBRILE PUERPERIUM | DEATHS | OUTCOME OF INFANT |
|-----------------|----------------|--------|------------------------|-----------------|---------------------------------|-------|-----------------------------------|---------|--------------------|--------|-------------------|
| | | | | | | | HOURS | MINUTES | | | |
| 1 | 24 | 6 | 200/130 | 4+ | 1.5 | 0 | 7 | 30 | 0 | 0 | Nonviable |
| 2 | 26 | 1 | 145/ 90 | 4+ | 0 | No. 4 | 0 | 30 | 1 | 0 | Nonviable |
| 3 | 37 | 1 | 160/ 98 | 4+ | 1 | No. 3 | 20 | 0 | 0 | 0 | Stillborn |
| 4 | 28 | 16 | 260/110 | 4+ | 1 | No. 4 | 3 | 30 | 0 | 0 | Stillborn |
| 5 | 34 | 1 | 210/130 | 4+ | 0 | No. 2 | 2 | 0 | 0 | 0 | Stillborn |
| 6 | 34 | 1 | 210/110 | 4+ | 1 | No. 4 | 4 | 30 | 1 | 1 | Stillborn |
| 7 | 26 | 1 | 180/130 | 4+ | 0 | No. 2 | 5 | 0 | 0 | 0 | Nonviable |

Transverse Presentations.—Ten patients in this group were treated by Braxton Hicks version (Table VI). There was only one primipara and she had a nonviable infant. The metreurynter was used in only one instance, as most of these patients entered the hospital in active labor, and the cervix permitted immediate Braxton Hicks version. The average time from version to delivery was 6 hours. The two patients who had stillborn infants also had marginal placenta previas.

TABLE VI. TRANSVERSE PRESENTATIONS

| | NUMBER OF CASES | PROLAPSED CORD OR ARM | BAG | AVERAGE TIME IN HOURS BETWEEN VERSION AND DELIVERY | MATERNAL MORTALITY | MATERNAL MORBIDITY |
|------------|-----------------|-----------------------|-----|--|--------------------|--------------------|
| Primipara* | 1 | 0 | 0 | 2 | 0 | 0 |
| Multipara | 9 | 1 | 1 | 7.5 | 0 | 2 |
| Total | 10 | 1 | 1 | 6 | 0 | 2 |

*Nonviable infant.

Viable Infants.—Of the one hundred and ten patients interrupted by Braxton Hicks version, fifty-seven had viable infants (Table VII). All patients who were 28 weeks pregnant or more by dates were considered to have viable infants, regardless of the weight of the child. This series represents many patients who were only 28 weeks pregnant or slightly over. Five infants were dead on admission. Eight patients delivered fetal monstrosities. There were twenty-three stillborn in-

infants (mostly fetuses of 28 weeks' gestation) and nine neonatal deaths. Twelve infants survived. The gross fetal mortality rate is 78.9 per cent. Excluding the five infants dead on admission and the eight fetal monstrosities, the corrected fetal mortality is 72.7 per cent. We consider this salvage good, particularly since this type of operation is not employed in the interest of the baby, except in the cases with transverse presentation.

TABLE VII. FETAL MORTALITY, BY INDICATION

| INDICATION | TOTAL VIABLE INFANTS | DEAD ON ADMIS- SION | STILL- BORN AND NEO- NATAL DEATHS | FETAL MORTALITY IN PER CENT | |
|--|----------------------------|---------------------------|---|--------------------------------|----------------|
| | | | | GROSS | COR- RECTED |
| Eclampsia | 4 | 0 | 4 | 100.0 | 100.0 |
| Severe pre-eclampsia | 16 | 2 | 10 | 75.0 | 71.4 |
| Placenta previa (all types) | 11 | 1 | 9 | 90.9 | 90.0 |
| Premature separation of placenta | 6 | 1 | 4 | 83.3 | 80.0 |
| Transverse presentation | 9 | 0 | 3 | 33.3 | 14.2 |
| Hydramnios with fetal monstrosi- ties | 8 | 0 | 8 | 100.0 | 100.0 |
| | | 0 | 2 | * | * |
| Chronic nephritis | 2 | | | | |
| Miscellaneous | 1 | 1 | 0 | * | * |
| Total | 57 | 5 | 40 | 78.9 | 72.7 |

*Small figures for rates.

It is interesting to compare the fetal mortality of the various groups:

1. The corrected fetal mortality rate in the antepartum bleeding cases is 80.0 per cent for seventeen viable infants (Table VIII). One infant was dead on admission, and one had multiple congenital defects. Only two infants survived.

TABLE VIII. FETAL MORTALITY IN ANTEPARTUM BLEEDING CASES

| TYPE OF CASE | TOTAL VIABLE INFANTS | DEAD ON ADMIS- SION | STILL- BORN | NEO- NATAL DEATHS | FETAL MORTALITY IN PER CENT | |
|-------------------------------------|----------------------------|---------------------------|----------------|-------------------------|--------------------------------|----------------|
| | | | | | GROSS | COR- RECTED |
| Placenta previa | 11 | 1 | 7 | 2 | 90.9 | 90.0 |
| Premature separation of placenta | 6 | 1 | 3 | 1 | 83.3 | 80.0 |
| Total | 17 | 2 | 10 | 3 | 88.2 | 86.6 |

2. The corrected fetal mortality rate in the toxemic group is 77.8 per cent (Table IX). None of the infants of the eclamptic patients survived. Four of the infants in the severe pre-eclampsia group survived. Two infants were dead on admission.

TABLE IX. FETAL MORTALITY IN TOXEMIAS

| TOXEMIA | TOTAL VIABLE INFANTS | DEAD ON ADMIS- SION | STILL- BORN | NEO- NATAL DEATHS | FETAL MORTALITY IN PER CENT | |
|----------------------|----------------------------|---------------------------|----------------|-------------------------|--------------------------------|----------------|
| | | | | | GROSS | COR- RECTED |
| Eclampsia | 4 | 0 | 4 | 0 | 100.0 | 100.0 |
| Severe pre-eclampsia | 16 | 2 | 6 | 4 | 75.0 | 71.4 |
| Total | 20 | 2 | 10 | 4 | 80.0 | 77.8 |

3. The corrected fetal mortality in the transverse presentation series for nine viable infants is 14.2 per cent, after excluding two stillborn infants delivered from patients with marginal placenta previa (Table X).

TABLE X. FETAL MORTALITY IN TRANSVERSE PRESENTATION

| | TOTAL VIABLE INFANTS | DEAD ON ADMIS- SION | STILL- BORN | NEO- NATAL DEATHS | FETAL MORTALITY IN PER CENT | |
|-----------------|----------------------------|---------------------------|----------------|-------------------------|--------------------------------|----------------|
| | | | | | GROSS | COR- RECTED |
| Multiparae only | 9 | 0 | 2 | 1 | 33.5 | 14.2* |

*Excluding two stillborn infants delivered from patients with marginal placenta previa.

Comment

The obstetrician is frequently confronted with the problem of termination of pregnancy in the latter months of gestation. The complications arising at this time usually entail considerable risk to the mother. Furthermore, salvage of the infant must oftentimes be considered. Good judgment and careful discernment are essential if the best interests of both are served to the fullest extent.

Many times the mother is subjected to the risk of a major abdominal procedure in the hope of obtaining a baby whose chance of survival is minimal. Prevalence of this attitude is exemplified in the results of an extensive state-wide survey presented by De Normandie.⁴ The mortality rate of infants delivered by means of cesarean section was 26.1 per cent. The maternal mortality rate which accompanied such a procedure was 11.7 per cent.

We realize that a fixed general policy for the proper treatment of such cases cannot be established, because even in obstetric clinics such uniformity of opinion does not exist. However, the obstetric surgeon should be versatily prepared to effect pelvic delivery in all obstetric complications where the viability of the infant is questionable. Therefore, we feel that the Braxton Hicks combined internal and podalic version is an operation which should be revived. It can be utilized not only for certain types of placenta previa but for various groups of cases, such as, severe toxemias of pregnancy, transverse positions, and hydramnios with certain types of monstrosities. In the hands of an experienced operator and with modifications in technique, seriously ill obstetric patients can be delivered safely.

Conclusions

1. One hundred and ten cases of Braxton Hicks combined internal and external versions were performed at the Boston Lying-in Hospital during an interim from 1930 through 1942.

2. The gross maternal mortality rate is 1.8 per cent. The morbidity rate is 20.0 per cent.

3. The gross fetal mortality rate is 78.9 per cent for fifty-seven viable infants; corrected, 72.7 per cent.

4. Certain modifications in technique are presented which, we believe, will: (1) simplify the operation, and (2) lower the morbidity rate.

5. We recommend the use of the Braxton Hicks bipolar version in patients with (1) *Placenta previa* (marginal and partial), when the infant has little chance of survival; (2) *Pregnancy toremias* (a) in severe pre-eclampsia, when the infant is nonviable or extremely premature; (b) in eclampsia, regardless of the infant's condition (except when cephalopelvic disproportion is present). (3) *Transverse presentations*, particularly in multiparas who have living children. (4) *Hydramnios* with fetal monstrosities.

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TWIN PREGNANCIES WITH ONE TWIN BLIGHTED

Report of Two Cases With Comparative Study of Cases in the Literature

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THE birth of a viable twin at or near term accompanied by the birth of a blighted fetus younger than the seventh month of gestation has been known for many years. Reference to such occurrences have been made in practically all of the older handbooks of midwifery, such as Guillemeau (1594),³⁰ Peu (1694),⁵⁷ Mauriceau (1695),³⁸ Chapman (1735),³⁸ Burton (1751),³⁸ Smellie (1752),³⁸ Albert Haller (*Elements of Physiology*, 1780),⁴¹ Denman (1821),³⁸ Dewees (1833),¹³⁹ Velpeau (1838),¹⁷⁰ Cruveilhier (1842),¹¹⁷ and Krause (1853).⁷¹ Ramsbotham¹¹⁰ says that this condition was remarked upon by Pliny. Despite the availability of this knowledge, many references to such occurrences during the last century are in the form of letters to the editors of medical journals briefly reporting such cases and asking for information concerning them. Examination of such brief reports supplies information primarily concerning the kind of labor, and secondarily the character of the dead fetus. Sometimes the age of the fetus was estimated, the age and parity of the mother were given together with a brief note on the character of the placenta and the umbilical cord. Occasionally, the sex, size and weight of the viable twin were given with the relative time of birth. In a number of cases, only the placenta and the dead twin were presented and described. One of the earliest comprehensive studies on the subject was presented for the doctorate of medicine at the University of Amsterdam by Luber⁵⁶ in 1811.

Dupoux³⁴ was probably the first to examine a part of the necrotic placenta under the microscope and report his findings. Following this time more attention was paid to the pathology of the placenta and with the introduction of the x-ray, determination of the age of the dead fetus as judged by the degree of ossification as well as by measurement was frequently reported. During the latter part of the nineteenth and the beginning of the present century cases were gathered to be used as theses. But in none of these theses was there a comprehensive survey in which the accumulated data were analyzed from quantitative as well as qualitative points of view.

In the present paper, I propose to give a brief description of two cases of this kind and, using these cases as a background, to present a quantitative and qualitative analysis of such data as have been available to me concerning numerous characteristics related to pregnancies

which have terminated at or near term with the birth of a viable child accompanied by a fetus which had died before the beginning of the seventh month of gestation. In presenting the data, I have tried to proceed from the more simple facts relating to the conditions under which the twins were born to the more complex anatomic and pathologic relations which have been reported concerning them. In making statistical contrasts, I have drawn freely on the reports of normal twins and single children given by Guttmacher,¹⁴⁷⁻¹⁴⁹ Greulich¹⁴⁶ and others.

In presenting my cases, I have adopted a topical method for brevity and clarity which will be applied to the analysis of the cases reported from the literature.

Reports of Cases

CASE 1.—This case is from the service of Dr. G. B. Byrd of Norfolk, Va. The fetus and its placenta were brought to the laboratory and the transcription of the case was furnished by Dr. Byrd. As mentioned above, the following topics have been based on this transcription. The mother was of the white race.

1. Chorionic character—dichorionic.
2. Age of mother—24 years.
3. Parity of mother—primipara.
4. Sex of viable twin—male.
5. Weight of viable twin—not given.
6. Time of birth of viable twin with reference to that of dead twin—immediately before.
7. Age of blighted twin in lunar months. The age was estimated from measurements of the upper arms, forearms, and legs because of the flattened and distorted condition of the fetus. Using these measurements, the age of the fetus was determined by contrasting these measurements with similar measurements of fetuses given by Scammon and Calkins.¹⁶¹ According to the measurements, the age of the fetus was 4.9 lunar months.
8. Character of preservation of the fetus. The fetus is of the flattened or papyraceous type. The degree of flattening and distortion is shown in a photograph of this fetus as it is viewed from the convex surface (Fig. 1). It is compressed from the opposite surface. As a consequence of the compression, the head is twisted so that the right side of the face is toward the left side of the body. Similar modifications of the orientation of the head have been described by Quadrat,¹⁰⁹ Edgar,³⁵ and Male.⁸⁸ The features are obliterated. The arms are bent on themselves and folded under the head, the left arm on the compressed concave side, and the right lying above the shoulders on the convex surface. The hands and fingers are well preserved and have been extended in the photograph. The thorax is flattened tangentially so that most of the ventral or anterior aspect of the body is on the concave surface. A glance at the picture will show how the ribs have been flattened. The sternum is slightly arched and protected the heart from flattening. The abdominal wall is flattened against the pelvis to such a degree that there is a slight rent in the midline through which part of the flattened intestinal coils protrude. Such a condition was observed by Wilson¹³⁴ in a flat fetus of the fourth month. The feet are

bent on the ankles, the ankles on the lower legs, and the lower legs on the thighs. The toes are well preserved and in the photograph have been extended together with the legs.

The whole surface of the body was grayish in color, and there was no bloating or swelling which according to Thomson¹⁶⁹ is characteristic of fetuses which have been macerated for 40 or 60 days or longer. The epidermis seems to be drawn down on the underlying bones in certain regions. There is occasional shredding of the epidermis and underlying corium. A section of the body wall was examined microscopically, and it was seen that the epidermis had shrunk to a thin line which might represent the remnants of the basement membrane. The underlying subcutanea is fibrous and the remnants of cells can be observed.



Fig. 1.—Photograph of papyraceous fetus. Case 1. Arms and legs are moved out from their abnormal positions. Note the rather thick umbilical cord to left of fetus. The head is completely twisted and face is directed to the right.

Such a condition has been recorded by Thomson¹⁶⁹ in macerated connective tissues. The morphology of the layers of muscle in the wall is maintained, and under high magnification, the striations of the muscle fibers are readily visible. Charrin²⁹ is the only one who has recorded such a preservation of muscle fibers in a dead fetus of this type. This kind of preservation seems to be quite remarkable in view of the fact, that the fetus had been dead for about four months and the muscles were devoid of circulating blood. It must be concluded that the little amniotic fluid which remained following compression

must have been a good preservative. Also the nuclei along the muscle fibers are well preserved in outline, although the chromatin does not stain with hematoxylin. The lamina propria of the peritoneum is fibrous, and there is a line formerly occupied by structureless membrane in place of the mesothelium.

Brief mention may be made of the conditions observed in the viscera. In the pelvic region, the compression has so obliterated the lower end of the body, that the sex could not be determined. The intestines are flattened, but their coils can be followed in the flattened abdominal cavity. Histologically, a section of the small intestine shows the characteristic muscular laminae in which the outlines of smooth muscle cells can be seen. The mucosa has sloughed into the lumen.

The right kidney has been obliterated by the compression, but the outline of the flattened left kidney can be seen. A section of this shows the fibrous capsule, but the tubules had shrunk and no details could be observed. The glomeruli had shrunk into masses of indeterminate structure. A small piece of the ureter taken with the kidney still shows a suggestion of transitional epithelium.

The stomach was not discernible; and the liver was evident only as a mass of fibrous material attached to the yellow inferior face of the diaphragm.

The lungs are flattened and markings suggestive of the lobes can be seen. A section of the lung contains remnants of the larger bronchi, in the walls of which, can be seen well-preserved cartilage plates. The cartilage cells are well preserved in outline, and show a granular cytoplasmic content which according to Thomson¹⁶⁹ is characteristic of degenerating connective tissue cells. Good preservation of cartilage in the trachea and lungs of papyraceous fetuses has been observed by Prestat¹⁰⁷ and Rigler.¹¹² The outlines of the larger vasa in the lungs are distinct, and remnants of smooth muscle cells can be seen in their walls. The alveoli and smaller ducts, however, appear as masses of necrotic cells without stainable boundaries or nuclei. Around the lungs, the ribs stand out sharply forming the framework of the pleural cavity. The pleura is yellow and tightly drawn over the ribs and extends deeply between them. The diaphragm and pericardial membrane are well preserved, and separate their respective cavities from each other.

The heart is remarkably well preserved and nonflattened, a condition noted by Rigler¹¹² in a dead fetus of the sixth month. Prestat¹⁰⁷ reported a well preserved although flattened heart in a four-month fetus. The heart in the present fetus was not flattened because the sternum formed a protective arch above it. There is no sign of blood in the pericardial cavity. Sections of the wall of the ventricle show maintenance of morphologic organization; muscle fibers and their nuclei retain their outlines. In the muscle fibers, delicate cross striations representing the Q discs can be seen. This histologic detail has never been reported before from a fetus which has been retained in utero after death for such a long period of time.

Since the features of the fetus were obliterated by the compression and the remainder of the body was soft, not shrivelled or dried, it would appear that this fetus can be classified as fetus papyraceus, partially macerated, but not mummified. Von Brücke¹³⁷ has shown that histologically bones, cartilage, muscle, brain and epidermis retain their characteristics for a long time in dead fetuses, even though the nuclei fail to stain and the cell boundaries are lost; and in connective tissues wandering cells abound.

9. Condition of mother during gestation—good health.

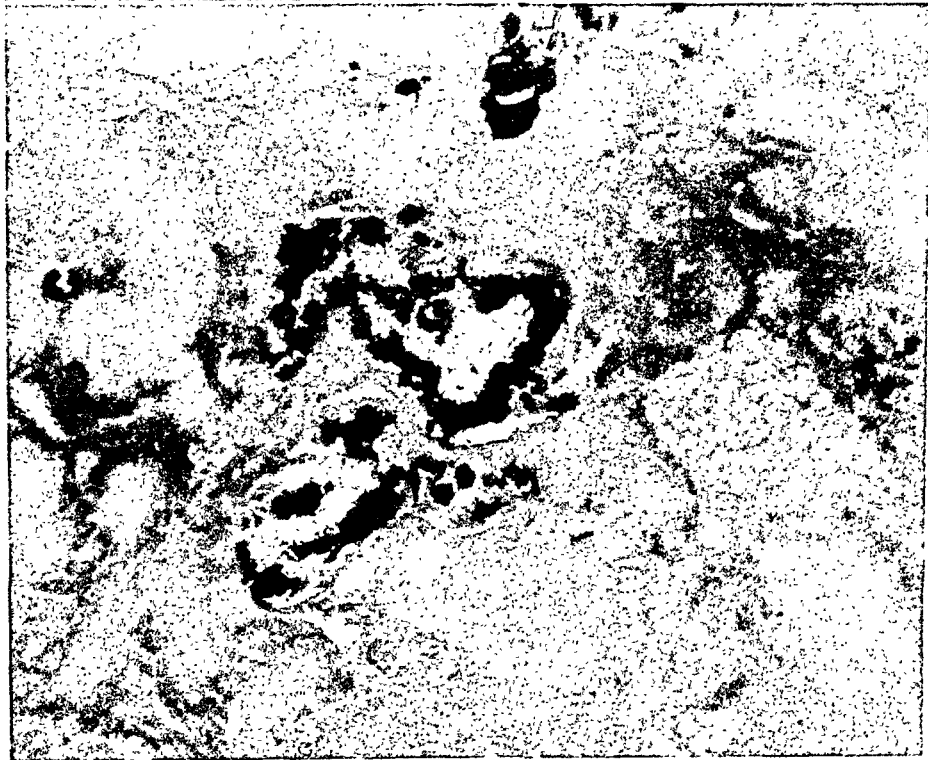
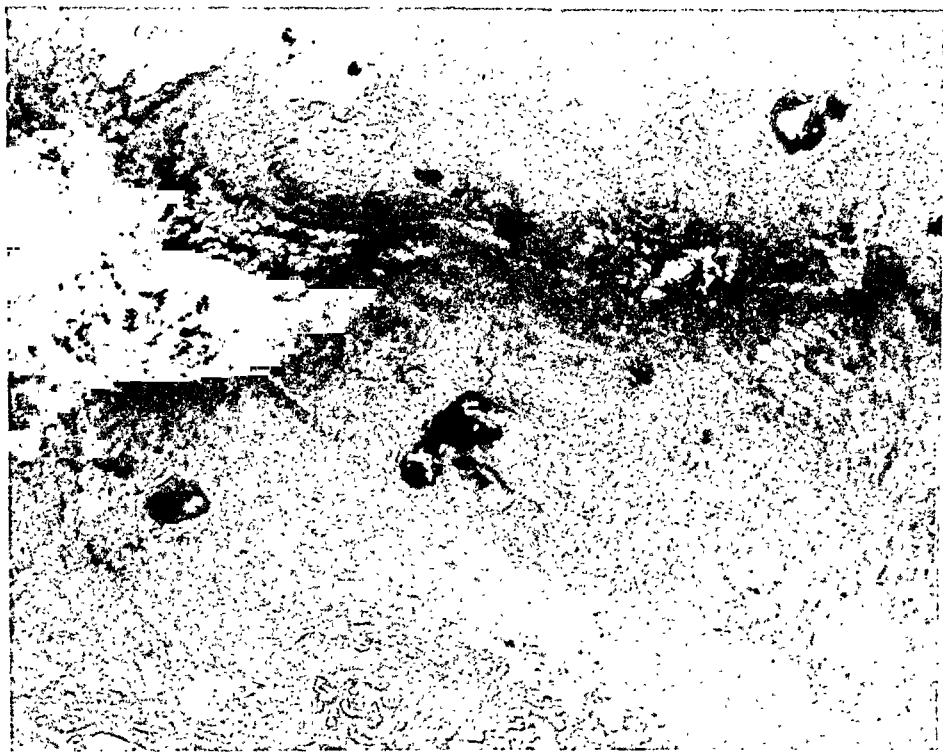
10. Characteristics of placenta. Grossly, the fetal placenta is hard. The fetal surface is covered by the closely adherent amnion, and has a glistening whitish color (Fig. 2). No traces of vasa can be seen. The maternal surface is yellow and the groups of hardened cotyledons can be observed. Dark patches occur here and there. There is no sign of any viable villi on the whole maternal surface. The placenta is concave toward the fetal surface, a condition produced apparently by the compression of the fetus. The umbilical cord is attached near one



Fig. 2.—Photograph of placentas from Case 1. Small placenta is from papyraceous fetus, larger one belongs to the viable twin.

margin about 5 mm. from the edge. It is thin, white and flat. No evidence of vasa could be seen in this piece grossly. The placenta measures 90 by 87 mm. in diameter. A section taken from the margin to the center shows it to be cone-shaped with the greatest thickness (14 mm.) in the center. From these measurements, the area of the fetal surface was estimated to be 61 square cm.; and treating it as a cone, the volume was estimated to be 29 cubic centimeters. The viable placenta measures 150 by 130 mm. in diameter and is 27 mm. thick at the center, and only slightly less in thickness at the margin. Its volume, treating it as a cylinder, was estimated to be 415 cubic centi-

A.



B.

Fig. 3.—Photomicrographs of a section of the placenta of the papyraceous fetus. Low power magnification showing remnants of villi and the masses of intervillous fibrin. The black masses are calcified areas. ($\times 35$.) *B*. High power magnification of small area of *A*, showing remnant of one villus; stroma light and enclosed in a ring of black calcified epithelium. Hematoxylin and eosin. ($\times 200$.)

meters. Hence, the volume of necrotic fetal placenta would be about 6.5 per cent of that of the viable.

The viable placenta shows no signs of gross necrosis. Its fetal surface shows the usual branching of the veins and arteries with deep bluish coloration as a background (Fig. 2). On the maternal surface, the cotyledons cannot be distinguished, and the whole surface appears as a bluish-gray mass in which a few yellow patches can be observed. It was quite compact when cut into, but was not hard and dense as is the fetal placenta. The fetal placenta was entirely distinct from the viable except at one small tangential point of contact. The fetal placenta with its attached compressed fetus enclosed in an intact amniotic membrane was delivered along with the viable placenta immediately following the birth of the viable child.

Sections of the fetal placenta show complete necrosis of the fetal elements. Traces of hyalinized villi can be seen, in between which are dense and loose masses of fibrin (Fig. 3A). There are no traces of chorionic epithelium. No traces of vasa are seen in the villi, and there is no sign of sclerosis of the vasa whose presence would be revealed by dense purple rings, which in material stained with hematoxylin is indicative of the presence of calcium. In many regions, one of which is shown in Fig. 3B, the hyaline villus is completely surrounded by a dense purplish ring which is interpreted as a deposit of insoluble calcium salts. These deposits seem to lie in the places formerly occupied by the chorionic epithelium. Sections through regions showing such deposits were incinerated according to the method of Scott¹⁶⁶ and a dense mass of ash was observed in the regions which showed purplish deposits in the preparations stained with hematoxylin and eosin. Treatment of ashed sections with hydrochloric and sulfuric acids showed the presence of gypsum crystals, which are presumed to be evidence for the presence of calcium in these deposits. This treatment was carried out because Schultz-Brauns and Schoenholz¹⁶⁵ hold that the presence of ash in heavy amounts in the regions formerly occupied by the chorionic epithelium is indicative of a pathologic process which started from the maternal surface. Following the initial necrosis of the chorionic epithelium, calcium which formerly was transmitted through the epithelium to the fetus could no longer follow this path because of lack of transportation facilities and hence, was increased in amount. On the other hand, if the fetus had died from intrinsic fetal causes, the calcium would show as rings in the walls of the fetal villous vasa and would be evidence of death from fetal arteriosclerosis. My observations led me to conclude from the above evidence that the placental condition, which is one of complete necrosis, had its inception in maternal conditions which caused necrosis of the chorionic epithelium, fibrin deposit and resulting calcium precipitation which in turn, prevented pabulum and oxygen from reaching the fetus. The sections viewed as a whole under the low power (Fig. 3A) resemble very closely the conditions shown in a section of a placenta of a blighted twin of the fourth month given by Adair.¹³⁵

In contrast with the fetal placenta, sections of the placenta of the viable twin show innumerable small villous terminations extending from large villi. Some necrotic villi were observed in this placenta and calcareous deposits were seen in the cores of these villi, but not in the epithelium. This kind of senile necrosis occurs normally in term placentas and starts with degeneration of the vasa in certain of the villi. Such degeneration is accompanied by calcareous deposits as the

vasa become obliterated by endarteritic or periarteritic changes. This is a well-known phenomenon and is said to be characteristic of senile placentas.¹⁶⁸

11. Characteristics of the umbilical cord. The umbilical cord of the fetus is 15 cm. long and extends from the umbilicus to the surface of the head on the side which has been compressed, and from there to the placenta. The region of the cord between the umbilicus and head is

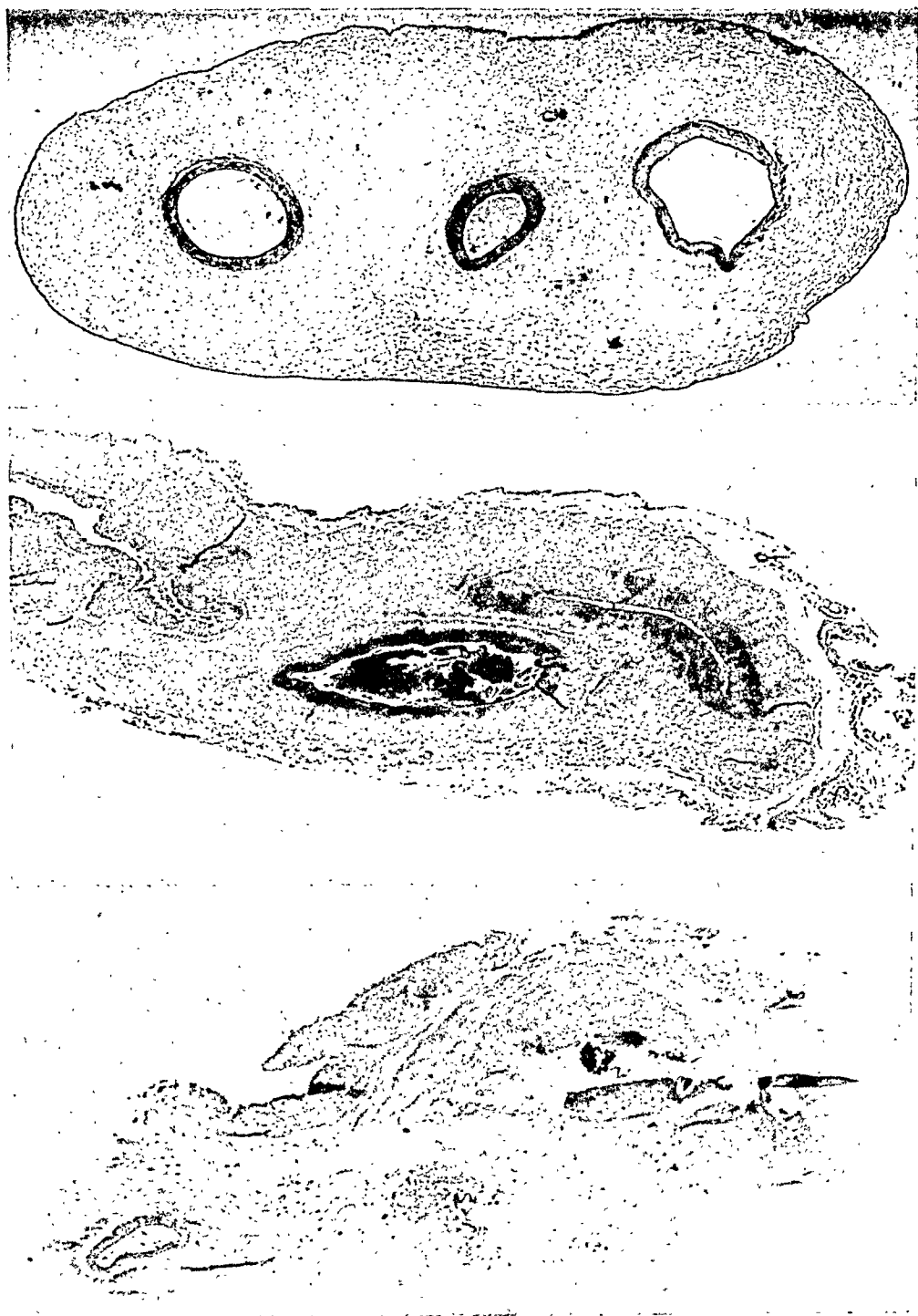


Fig. 4.—Photomicrographs of transverse sections of: A, umbilical cord of normal fetus of fourth month; B, umbilical cord of papyraceous fetus in region of least degeneration; and C, umbilical cord of same papyraceous fetus in region of greatest degeneration. Hematoxylin and eosin. (X20.)

flattened, but sections show it to have retained its outline with the amnion loosely attached to the underlying stroma (Fig. 4B). The stroma of mucoid connective tissue is quite fibrous, is arranged around the vasa in concentric layers, and is almost tendinous in character. In between the fibers can be seen the outlines of necrotic cells, most of which have contracted. The vasa are flattened, but have retained their outlines, and the arrangement of muscle fibers in the medias are easily recognized. There is no sign of sclerosis in these vasa. A large clot of fibrin and blood corpuscles is present in the lumen of the umbilical vein, and in one artery there is a trace of a clot. This part of the cord is 3 cm. long and the diameters are 2 mm. and 7 mm., respectively. The media of the arteries averaged 1.0 mm. in thickness and that of the vein 0.4 millimeter. The lumens of the arteries are compressed, and that of the vein open with a clotted content.

The appearance of a section of that part of the umbilical cord which extends from the adhesion on the head to the placenta for a distance of 12 cm. is quite degenerate as compared with the part just described. In this region, the cord is very flat and measures 4.0 by 1.5 mm. in diameter (Fig. 4C). It is incomplete in several places, and only one artery has retained its outline. The other artery and the vein have almost completely degenerated. The muscle of the media of the artery which has been preserved is shrunk and disorganized. There is no blood or clot in the lumen, or in the region of the degenerated vasa. The surrounding connective tissue is fibrous and dense, but shows less organization than the connective tissue of the other part.

For contrast with this umbilical cord, the cord of a normal fetus of 110 mm. C-R length (age about 4.3 months) was sectioned. The cord is flat and measures 6.3 by 2.7 mm. in diameter (Fig. 4A). The amnion is closely applied to the underlying stroma which is composed of the usual mucoid connective tissue cells with few fibrils irregularly arranged. This condition is in contrast with the closely packed concentric arrangement of the fibrils in the better preserved section of the cord of the papyraceous fetus. The media of the arteries average 0.5 mm. in thickness, and that of the vein 0.4 millimeter. These measurements are not significantly different from those of the same parts of the umbilical arteries and vein of the dead fetus. Hence, it appears that the better preserved part of the cord of the dead fetus has not changed much in size or arrangement of parts during the period of intrauterine retention even though the tissues are dead.

The histologic differences characteristic of the two parts of the umbilical cord of the papyraceous fetus indicate that the necrotic changes have been of longer duration in the part between the placenta and the head than in that part between the head and the umbilicus. It is concluded that this is evidence that the necrotic process started in the placenta and progressed toward the fetus, and that with the death of the fetus, the cord was compressed between the head of the fetus and the head of its viable twin, thereby slowing down the progress of necrosis in the part between the compression and the umbilicus. I think that there is no evidence for the view that the compression of the cord preceded the death of the fetus, otherwise that part of the cord nearest the fetus would show a greater degree of degeneration than that between the head and the placenta.

12. Summary. The evidence presented from a study of the placenta and umbilical cord of this fetus suggests that the fetus died because

of placental necrosis induced by some change in the maternal blood. Following death, the fetus was flattened by pressure from its twin and following this flattening a maceration process started, which although progressing to a certain degree did not completely destroy the histologic characteristics of certain organs, particularly the heart and muscle of the body wall.

Unfortunately, there is no record of the amount of fluid present in the amniotic sac of this fetus. Some fluid must have been present, since the fetus is not mummified, a condition which is said to occur when the fluid is absorbed following fetal death. The excellent preservation of histologic relation of certain of the organs and particularly of the muscle striations implies that the fluid which was present was an excellent preservative.

Another unfortunate hiatus is lack of information concerning the type of presentation of the viable twin. This information would be used in the discussion of causes of compression in the latter part of this paper.

The fetus can be called a fetus papyraceus with a degree of maceration. It shows no signs of mummification. Measurements of certain dimensions place the time of its death at 4.9 lunar months.

CASE 2.—The record of this case came from the Obstetric Service of the University of Virginia Hospital. The clinical history was given by Drs. Kight and Schneider. Dr. Kight has kindly furnished me with a transcription of the record from which the data in the following topics are taken. Neither fetus nor placenta was available. The mother was of the Negro race.

1. Chorionic character—monochorial with two amnions.
2. Age of mother—18 years.
3. Parity of mother—primipara.
4. Sex of viable twin—male.
5. Weight of viable twin—2,050 grams.
6. Time of birth of viable twin with reference to that of dead fetus—immediately before. Viable twin delivered in left occipito-anterior position.
7. Age of blighted twin in lunar months—not known, but rather small.
8. Character of preservation of fetus—fetus papyraceus, flattened and macerated.
9. Condition of mother during gestation. First day of last period, November 10, 1942. Bleeding in February, 1943, for one week, otherwise health good. Such bleeding could have been coincident with time of death of the fetus as has been recorded in a number of cases of this kind.^{5, 9, 34, 54, 61, 70} Since the fetus was not measured, this relation cannot be checked.
10. Characteristics of the placenta. Single placenta, one chorion and two amnions. Sketch on hospital record shows an area equal to about $\frac{1}{6}$ of the placenta which was hard and fibrosed. The fetal cord was attached to this area. No record of further examination of placenta.
11. Umbilical cord—thin and flat. Cord of viable fetus, eccentric attachment; fetal cord attached near opposite margin.
12. Summary. Fetus papyraceus macerated, monochorial twin with separate amnion; placenta in region of fetal cord necrotic. Apparently, from the history, there was detachment of the placenta in the part

belonging to the fetus at the beginning of the fourth month of gestation. Otherwise, mother's health good. Premature labor beginning of seventh month with birth of viable fetus and this papyraceous fetus. Labor brought on by sudden flow of amniotic fluid from vagina while riding in auto. From the data nothing can be learned as to whether death was caused by increased activity of the other twin, or by local changes in the placenta in region of fetal attachment. The presence of the dead fetus and the necrotic part of the placenta apparently had no effect on the mother's health. Viable child presented in left occipito-anterior position.

Review of Literature

Analyses of reports of cases of twins in which one was born alive at or near term and the other, which died before the seventh month of pregnancy, was born at or about the same time as the viable twin.

In the following sections, the data from other authors relating to the topics listed in the reports of the two cases cited here, will be presented. Unfortunately, although I have examined most of the reported cases, there are about 30 titles to which I had reference, but which could not be obtained. I have examined the records of 148 cases. With the addition of the two cases reported here, the total number on which the following data are based is 150. However, even such a number of cases is probably mere sampling of the conditions which really occur since Guttmacher¹⁴⁸ has recorded that in 500 twin pregnancies there were 11 cases of fetus papyraceus.

As a matter of interest, but not of particular importance, I include here the references as reported by country. These are as follows: United States, 32; France, 31; England, 27; Germany, 27; Russia, 5; Hungary, 4; Italy, 4; Argentina, Belgium, Holland and Scotland, 3 each; Austria, Czechoslovakia, China, Finland, Indo-China, Ireland, India, Poland, South Africa, Sweden, Switzerland and Turkey, one each. A total of 154 references. Of these references I have examined 133, from which I have gathered data on 148 cases. In several of the more comprehensive articles, such as theses, several cases are reviewed and these frequently overlap. I have found that such a title as "fetus papyraceus" does not always refer to twins if this is the only title given, as the occurrence of this condition in triplets has been reported under this title alone. Furthermore, such a title does not mean that the unmodified fetus was born alive e.g., in 28 cases of fetus papyraceus reviewed by Lampert⁷⁶ only 16 were in the twin classification which I am using here.

The most comprehensive papers which I have seen have been presented by Prestat,¹⁰⁷ Dupoux,³⁴ Rigler,¹¹² Ethridge,³⁸ Cosentina,²² Hélot,⁵⁵ Peckham-Murray,¹⁰⁴ Pujol,¹⁰⁸ Danel,²⁷ Reynès,¹¹¹ von Lichem,⁴⁴ Acconci,² Hähnel,⁴⁸ Schneider,¹¹⁷ Guggisberg,⁴⁷ Lampert,⁷⁶ Aburel,² Bernhart,¹⁰ and Szendi.¹²⁷

In the following sections the data are gathered under the headings given in the description of my cases, and these cases are included with

those gathered from the literature. In order to prevent repetition and yet make the data understandable, the term blighted fetus as used in the following pages refers to a fetus which has died in utero before the seventh lunar month, and has been retained in utero with its viable twin until just before or after the birth of the latter. The terms monochorial and dichorial twins are used throughout, because this diagnosis has been made from the characteristics of the placentas.

1. *Chorial Character of the Blighted Fetuses.*—Total cases 141.

Monochorial, 48 (34 per cent).

Dichorial, 93 (66 per cent).

These data show that in the reported cases there is a higher incidence of blighting in dichorial than in monochorial twins. According to Hähnel,⁴⁸ blighted twins are more common in monochorial than in dichorial twins, but no quantitative data are used to support this view. Also Peckham-Murray¹⁰⁴ states that the majority of blighted twins are those with only one placenta. The data presented here reverse these conclusions. However, examination of the data on the distribution of monochorial and dichorial twins in twin populations shows that the distribution of blighted twins is proportional to the distribution of monochorial and dichorial as reported by several investigators. The data agree closely with those presented by Kleine,¹⁵³ 36 per cent monochorial; Szendi,¹²⁷ 34 per cent; Zangenmeister,¹⁴³ 30 to 35 per cent; Hoehne,¹⁴³ 33 per cent; McElroy,¹⁴³ 37.3 per cent; and with the theoretical incidence calculated by Jenkins and Gwin,¹⁵⁰ about 36 per cent. The percentage of monochorial twinning is greater than the percentages given by Goecke,¹⁴³ 16 per cent; Orel,¹⁴³ 21 to 26 per cent; Von Verschner,¹⁴³ 23 to 25 per cent; Olshauser,¹⁴³ 25 per cent; Ahfeld,¹⁴³ 16 per cent; Guttmacher,¹⁴⁷ 25.7 per cent; and Greulich,¹⁴⁶ 18.17 per cent. It is less than that given by Komai and Fukuoka¹⁵¹ (56 per cent). In view of these distributions of monochorial twins in a number of twin populations, it is concluded that one of dichorial twins is not more often blighted than is one of monochorial twins, but the difference in incidence is due to the distributions of the two types of twinning in twin populations.

There were only three cases in which the monochorial twins were mono-amniotic.^{7, 11, 61}

2. *Age of Mother in Relation to Blighted Twins.* Eighty-four cases.

TABLE I. AGE OF MOTHER AND CHORIAL CHARACTER OF BLIGHTED TWINS, 84 CASES

| CHORIAL CHARACTER | | AGE OF MOTHER IN YEARS | | | | | | TOTALS |
|-------------------|-------------|------------------------|----------|----------|----------|----------|---------|--------|
| | | UNDER 20 | 20 TO 25 | 25 TO 30 | 30 TO 35 | 35 TO 40 | OVER 40 | |
| Number | Monochorial | 5 | 8 | 10 | 6 | 3 | 0 | 32 |
| | Dichorial | 0 | 9 | 13 | 19 | 4 | 7 | 52 |
| Per cent | Monochorial | 15.6 | 25.0 | 31.3 | 18.7 | 9.4 | 0 | 100 |
| | Dichorial | 0 | 17.4 | 25.0 | 36.4 | 7.7 | 13.5 | 100 |

Table I shows that when the ages of the mothers in which one of the twins is blighted are compared with regard to chorial character, there is a trend in the direction of youth on the part of mothers of monochorial twins. Up to the age of 30 years, there is a greater percentage of blighting when the twins are monochorial; and the reverse when they are dichorial. These distributions were tested to see whether they were due to the distributions of the twins of each type in the general population at these ages, or whether the blighting was related to age alone. For purposes of these contrasts, two tables have been made from the data available in the literature.

TABLE II. PERCENTAGE INCIDENCE OF BLIGHTED MONOCHORIAL TWINS AND AGE OF MOTHERS CONTRASTED WITH DISTRIBUTIONS OF MONOCHORIAL TWINS ON MOTHERS' AGE IN NORMAL MONOCHORIAL TWIN POPULATIONS

| SOURCE OF DATA | AGE OF MOTHERS IN YEARS | | | | | |
|-------------------------------------|-------------------------|----------|----------|----------|----------|---------|
| | UNDER 20 | 20 TO 25 | 25 TO 30 | 30 TO 35 | 35 TO 40 | OVER 40 |
| Blighted (Present) | 15.6 | 25.0 | 31.2 | 18.7 | 9.4 | 0 |
| Normal (Guttmacher ¹⁴⁷) | 18.5 | 32.8 | 21.0 | 15.1 | 7.6 | 5.0 |
| Normal (Greulich ¹⁴⁶) | 19.0 | 31.0 | 22.0 | 20.0 | 12.0 | 4.0 |

In Table II the data from Guttmacher¹⁴⁷ and Greulich¹⁴⁶ indicate that the distribution of the blighted twins in relation to mother's age is probably proportional to the incidences of monochorial twins in mothers of these age groups, and that this distribution is not so much related to the age of the mother as it is to the incidence of monochorial twins in mothers of these age groups. The greatest degree of blighting occurs in those ages where the monochorial twins are most numerous. Thus, the trend to youth in mothers of blighted twins shown in Table I, is the result of the tendency of the younger mothers to have more monochorial twins than older mothers. The chi-square test of these data supports this view, as there is no significant deviation from expectation except in the older group where the incidence of blighting is less than expected.

TABLE III. PERCENTAGE INCIDENCE OF BLIGHTED DICHORIAL TWINS AND AGE OF MOTHERS CONTRASTED WITH DISTRIBUTIONS OF DICHORIAL TWINS ON MOTHERS' AGE IN NORMAL DICHORIAL TWIN POPULATIONS

| SOURCE OF DATA | AGE OF MOTHERS IN YEARS | | | | | |
|-------------------------------------|-------------------------|----------|----------|----------|----------|---------|
| | UNDER 20 | 20 TO 25 | 25 TO 30 | 30 TO 35 | 35 TO 40 | OVER 40 |
| Blighted (Present) | 0 | 17.4 | 25.0 | 36.5 | 7.7 | 13.5 |
| Normal (Guttmacher ¹⁴⁷) | 9.3 | 22.3 | 25.4 | 22.1 | 19.2 | 1.7 |
| Normal (Greulich ¹⁴⁶) | 6.0 | 22.0 | 26.0 | 26.0 | 18.0 | 4.0 |

Table III shows that blighting of one twin in dichorial pregnancies occurs less often than would be expected in mothers under 20 years of age, and from 35 to 40 years; and it is proportional to the distribution of normal twins in mothers from 20 to 30 years of age; while it is greater than expectation in the 30 to 35-year group and in those over

40 years of age. The dichorial group shows more variation from expectation than the monochorial group, hence, the chi-square test has been applied to this table. In this contrast, the data of Guttmacher and Greulich have been averaged, and the average incidences have been contrasted with the incidences given in the present data.

TABLE IV. CHI-SQUARE TEST FOR DISTRIBUTION OF BLIGHTING IN DICHORIAL TWINS AND AGE OF MOTHERS

| SOURCE OF DATA | AGE OF MOTHER IN YEARS | | | | | |
|----------------------------------|------------------------|----------|----------|----------|----------|---------|
| | UNDER 20 | 20 TO 25 | 25 TO 30 | 30 TO 35 | 35 TO 40 | OVER 40 |
| Blighted (Present) | 0 | 17.4 | 25.0 | 36.5 | 7.7 | 13.5 |
| Normal (Guttmacher and Greulich) | 7.5 | 22.0 | 25.0 | 24.0 | 19.0 | 3.0 |
| Chi-square | 7.5 | 0.96 | 0.0 | 8.5 | 8.75 | 36.6 |

Since the total chi-square value in Table IV is 62.31, and the number of classes (n) is 5, the probability that in the whole group the blighting is not proportional to the distribution of the twins in all classes is very significant, less than 0.01.¹⁴⁰ Examination of the table, however, with reference to the several classes, shows that the large total chi-square value is due to variation from expectancy in four of the six classes. In the under 20-year class, blighting is significantly less than would be expected. It is proportional to the population in the 20- to 25- and 25- to 30-year classes; is significantly greater in the 30- to 35-year class and notably less in the 35- to 40-year class. Finally, it is significantly greater than expectation in mothers, 40 years of age or older. Hence, it is concluded that in dichorial gestations, there is more chance of one twin being blighted if the mothers are older than 40 years, and less chance if they are younger.

When the results given here are used in contrasting blighting in dichorial and monochorial twins in relation to the age of the mother, it is seen that there is less relation between blighting and age of mother in monochorial than in dichorial twins. In the dichorial group, there are two classes of mothers in which blighting is greater than expected, while in the monochorial group, there is none. Thus, the age of the mother seems to be definitely concerned with survival of both members of a twin pregnancy only when the twins are dichorial and the mother is either from 30 to 35 years, or over 40 years of age.

3 A. *Blighting in Relation to Parity of Mother and Chorial Character of Pregnancy.*

The data in this section were obtained from the records given in 101 cases. In Table V the numerical and percentage incidences of the monochorial and dichorial pregnancies are listed. The data so listed were tested for significance with reference to the incidences of monochorial and dichorial twins and parity of mothers in normal twins as given by Guttmacher.¹⁴⁷ In the latter tables (Tables VI and VII), the chi-square test for agreement with expectations has been applied.

TABLE V. INCIDENCE OF BLIGHTED TWINS AND PARITY OF MOTHER, 101 CASES

| CHORIAL CHARACTER | | PARITY OF MOTHER | | | | | |
|-------------------|-------------|------------------|------|------|-----|------------|--------|
| | | 1 | 2 | 3 | 4 | 5 AND OVER | TOTALS |
| Number | Monochorial | 16 | 4 | 6 | 2 | 8 | 36 |
| | Dichorial | 13 | 14 | 5 | 4 | 29 | 65 |
| Per cent | Monochorial | 44.5 | 11.1 | 16.6 | 5.6 | 22.2 | 100 |
| | Dichorial | 20.0 | 21.6 | 7.7 | 6.2 | 44.5 | 100 |

When the values in the different para groups shown in Table V are contrasted, it will be seen that there seem to be relatively more blighted monochorial twins in primiparas and in the para 3 class than in these same classes in the dichorial group. Whereas more dichorial than monochorial twins seem to have been blighted in the para 2 and para 5 classes. These differences, however, have no significance unless they are tested against the proportions of monochorial and dichorial twins in twin populations at different degrees of parity. Hence, tests have been made by the chi-square method using the data of Guttmacher¹⁴⁷ on the incidences of monochorial and dichorial normal twins in relation to parity. These data are presented in the following tables (Tables VI and VII).

TABLE VI. CHI-SQUARE TEST OF PERCENTAGE INCIDENCE OF BLIGHTED MONOCHORIAL TWINS AGAINST NORMAL MONOCHORIAL TWINS AND PARITY OF MOTHER

| SOURCE OF DATA | PARITY OF MOTHER | | | | | |
|-------------------------------------|------------------|------|------|------|------------|----------------------------|
| | 1 | 2 | 3 | 4 | 5 AND OVER | |
| Blighted (Present) | 44.5 | 11.1 | 16.6 | 5.6 | 22.2 | Total chi-square, 15.81 |
| Normal (Guttmacher ¹⁴⁷) | 31.9 | 17.6 | 11.8 | 16.0 | 22.7 | |
| Chi-square | 5.0 | 2.4 | 1.9 | 6.5 | 0.01 | |

When the total chi-square is 15.81 and n equals 4, the probability that the incidence of blighting differs from expected proportions is significant ($P = 0.01$).¹⁴⁰ However, examination of Table VI shows that in the separate para classes, the primiparas have more blighting than should be expected, and there is less blighting than was expected in the para 4 class. Except for these differences, the distribution shows that blighting is proportional to the incidence of normal monochorial twins in the several para classes. Thus, in only the primiparas is there greater blighting than should be expected if the incidence of blighted twins depended only on the distributions of the normal twins in the several para classes. Such a distribution suggests that there is some factor or factors which make monochorial twins susceptible to blighting when the mother is a primipara.

Since in Table VII the total chi-square is 11.8 and n is 4, the distributions of the blighted dichorial twins depart significantly from expectations. However, examination of the table shows that this deviation is caused entirely by the incidence of blighting in the para 2 group.

TABLE VII. CHI-SQUARE TEST OF PERCENTAGE INCIDENCE OF BLIGHTED DICHORIAL TWINS AGAINST NORMAL DICHORIAL TWINS AND PARITY OF MOTHER

| SOURCE OF DATA | PARITY OF MOTHER | | | | | |
|-------------------------------------|------------------|------|------|------|------------|------------------------|
| | 1 | 2 | 3 | 4 | 5 AND OVER | |
| Blighted (Present) | 20.0 | 21.6 | 7.7 | 6.2 | 44.5 | |
| Normal (Guttmacher ¹⁴⁷) | 20.2 | 11.8 | 12.6 | 10.6 | 44.8 | |
| Chi-square | 0.002 | 8.0 | 1.9 | 1.9 | 0.002 | Total chi-square, 11.8 |

There is significantly more blighting in this class than was expected. Hence, it is concluded that except for the para 2 class, the parity of the mother does not influence the blighting of dichorial twins and that blighting is proportional to the distribution of the normal dichorial twins in the several classes of parity.

When the data obtained from Tables VI and VII are contrasted and reference is made to Table V, it is seen that the high incidence of blighting in monochoiral twins of primiparous mothers is significantly greater than that in primiparas with dichorial twins. Also, the greater incidence of blighting in the dichorial twins of para 2 mothers is significantly greater than in monochoiral twins of the same class of mothers. In the other classes of mothers in both monochoiral and dichorial pregnancies, the incidences of blighting are proportional to the population of twins of these classes, or even less than expected proportions.

The most important conclusion from these comparative data is the fact that blighting of one twin may occur more often than should be expected in monochoiral pregnancies of primiparous mothers.

3 B. *Death of One Twin in Twin Pregnancies and Parity of the Mother contrasted With Death of Fetuses in Single Pregnancies and Parity of Mother.*

In this section an attempt has been made to test the expectancy of death of one twin in twin pregnancies in relation to parity by contrasting these data with those for the deaths of fetuses in relation to parity in single pregnancies. The data used for the single fetuses are those of Grier¹⁴⁵ obtained from an analysis of the incidence of fetal death in relation to parity in 4,668 consecutive deliveries. There were 225 fetal deaths. The data on the blighted fetuses are the combined figures of incidences of monochoiral and dichorial twins on parity given in Table V.

TABLE VIII. CHI-SQUARE TEST OF BLIGHTING OF ONE TWIN IN TWIN PREGNANCIES AND PARITY AS CONTRASTED WITH FETAL AND PARITY IN SINGLE PREGNANCIES. DATA GIVEN TO NEAREST 1.0 PER CENT.

| GROUP | PARITY OF MOTHER | | | | |
|----------------|------------------|-----|-----|------|------------|
| | 1 | 2 | 3 | 4 | 5 AND OVER |
| Blighted twins | 29 | 18 | 11 | 6 | 37 |
| Single fetuses | 47 | 26 | 13 | 5 | 7 |
| Chi-square | 1.1 | 2.4 | 0.3 | 0.01 | 129.0 |

Table VIII shows that by the use of the chi-square method, no significant differences are revealed between the incidences of death of one of twins and of single fetuses in any degrees of parity except in the para 5 and over class of mothers. In this class, the percentage of death of one of twins is significantly greater than that for single births. But before making a final conclusion, the data of Guttmacher¹⁴⁷ on the incidence of twin births in this class were consulted, and from these data it appears that the apparently great difference is, in large part, caused by the relatively greater number of twins born to mothers of this class as contrasted with the mothers in the other classes. Whereas in single pregnancies the greatest number of births is in primiparas, in twins it is in the five or over pregnancy class, and so population differences must be borne in mind when making such contrasts as above. Even if this population difference exists between the different parous classes, it still seems possible to conclude that the relative incidence of blighting of one fetus in twin pregnancies is significantly greater than the incidence of death of single fetuses in single pregnancies, when in both cases the mothers are in the fifth or higher degree of parity.

4. Sex of the Viable Twin of Twin Pregnancies in which one is Blighted.

In 142 cases in which the chorial characters of the twins were given, the sex of the viable twin was recorded in only 71 cases. The distribution is as follows: Monochorial: male, 19 (39.6 per cent); female, 10 (20.8 per cent); sex not given, 19 (39.6 per cent). Dichorial: male, 25 (27.8 per cent); female 22, (18.9 per cent); sex not given, 48 (53.3 per cent).

These data show that in this group of blighted twins, the percentage of blighting is greater in those sets in which the surviving twin is male in both monochorial and dichorial pregnancies. These data tend to support the view of Aburel² that female monochorial twins survive more often than male, and of Pringle (cited by Aburel), that mortality is less among female pairs of twins. However, because of the high percentage of cases in which no sex was recorded, the evidence for this view may not be statistically significant.

The sex ratio in U.S. Vital Statistics for 1937,¹⁷² for one twin born alive is: viable twin males, 642 (53.5 per cent); females, 554 (46.5 per cent). The data in the present paper grouping all twins together show twin pregnancies in which males survive to be 44 cases (62.0 per cent); and females, 27 (38 per cent), a distribution which is not significantly different from the U.S. Vital Statistics. Hence these data support the view expressed above that twins, of which one is male, are more susceptible to blighting than those in which one is female.

5. Weights of Surviving Viable Twins in Contrast With Each Other; With the Weights of Twins in Which Both Survive; and With the Weights of Single Births.

A. Weights of viable survivors of monochorial and dichorial twins in which one member of the pair has died before the seventh month of pregnancy. Data given as averages with standard errors (v) of these averages.

1. Monochorial (20 cases); average weight, $3,550 \pm 180$ grams.
2. Dichorial (31 cases); average weight, $3,100 \pm 150$ grams.

TABLE IX. CONTRAST BY THE CHI-SQUARE METHOD OF VIABLE TWIN SURVIVORS OF BLIGHTED TWIN PREGNANCIES BY WEIGHT WITH WEIGHTS OF TWINS IN WHICH BOTH SURVIVED (DATA ON THE LATTER FROM POTTER AND CRUNDEN¹⁶¹)

| CLASS | VIABLE SURVIVORS PERCENTAGE | BOTH TWINS VIABLE PERCENTAGE | CHI-SQUARE |
|----------------------|--------------------------------|------------------------------------|------------|
| 500 to 1,000 grams | 0 | 5.2 | 5.2 |
| 1,000 to 2,500 grams | 15.7 | 43.6 | 17.9 |
| 2,500 to 6,000 grams | 84.3 | 51.2 | 21.4 |

Contrast of the above shows that monochorial twin survivors average 450 ± 740 grams heavier than dichorial. This difference is not statistically significant.

B. Weights of the same groups classified by sex.

1. Monochorial males (9 cases); average weight, $3,720 \pm 320$ grams.
2. Monochorial females (5 cases); average weight, $3,200 \pm 360$ grams.
3. Dichorial males (11 cases); average weight, $3,080 \pm 190$ grams.
4. Dichorial females (9 cases); average weight, $3,040 \pm 190$ grams.

Contrasting the above data by the standard error method for check on significant differences shows that the monochorial males average 520 ± 485 grams heavier than monochorial females. This difference is not statistically significant.¹⁴⁰

Monochorial males average 640 ± 375 grams heavier than dichorial males. This difference is not statistically significant.

Monochorial females average 160 ± 400 grams heavier than dichorial females, but this difference in weight is not statistically significant.

In brief, the above data show that there are no statistically significant differences between the weights of viable twin survivors of monochorial and dichorial pregnancies; nor is there any difference between the weights of males and females.

C. Weights of viable twin survivors of twin pregnancies in which one twin has died before the seventh month, compared with the weights of viable twins in which both survive.

1. Average weight of viable twins, both surviving, 2,391 grams (333 pairs, Potter and Crunden¹⁶¹).
2. Average weight of viable survivor of blighted twin pregnancies (51 cases), 3,280 grams.

These data show that the viable survivors of blighted twin pregnancies are on the average 889 grams heavier than twins in which both are viable.

In order to see how the weights of these two groups compared in distribution, they were classified into the groups listed by Potter and Crunden.¹⁶¹

Table IX shows that there are fewer viable survivors of blighted twin pregnancies in the lower weight classes, and more in the upper weight class, than there are in these classes in twin pregnancies when both twins survive. In all classes when analyzed by the chi-square method, the departure from expectation is statistically significant. Hence, it is concluded from these data that the surviving twin of a twin pregnancy in which one twin is blighted is more likely to be heavier than either one of twins where both survive. According to Statz as cited by Newman,¹⁵⁸ increase in weight of the surviving twin is probably due to the appropriation of the nutritive material by this twin at the expense of its companion. This is particularly true of monochorial twins.

D. Contrast of the weights of viable twin survivors with weights of single births in previable, premature and normal birth weight classes. The data for the weights of single births are from Potter and Crunden,¹⁶¹ and are contrasted with the weights of viable twin survivors given in the previous sections.

TABLE X. CONTRASTS BY THE CHI-SQUARE METHOD OF WEIGHTS OF VIABLE TWIN SURVIVORS WITH THOSE OF SINGLE BIRTHS

| CLASS | SINGLE BIRTHS PERCENTAGE | VIABLE SURVIVORS PERCENTAGE | CHI-SQUARE |
|---------------------------------|-----------------------------|-----------------------------------|------------|
| Previable, 400 to 1,000 grams | 0.52 | 0 | 0.52 |
| Premature, 1,000 to 2,500 grams | 5.8 | 15.7 | 17.0 |
| Mature, 2,500 to 6,000 grams | 93.6 | 84.3 | 0.92 |
| Total | | | 18.42 |

The total chi-square value of 18.42 in Table X indicates that the deviation from expectancy is statistically significant. Practically all of this high chi-square value is caused by the greater number of surviving twins in the premature class than would be expected if the distribution was proportional to the distribution of the weights of single births. Hence, it is concluded that surviving twins of blighted twin pregnancies have a higher incidence of premature birth than do children of single pregnancies. According to Guttmacher¹⁴⁹ in 573 twin pregnancies, $\frac{3}{8}$ of the number were in the premature class. This fact combined with the data given in this section and in section C, suggests that there is a greater tendency for the surviving twin of twin pregnancies in which one has died before the seventh month to approach

the average birth weights of single births in the mature class, than do twins in which both survive.

6. *Time of Birth of Viable Twin in Relation to That of Dead Twin.*

The data in this section were obtained from records of 46 monochorial and 84 dichorial pregnancies. These data are summarized in Table XI.

TABLE XI. CONTRAST OF TIME OF BIRTH OF MONOCHORIAL AND DICHORIAL VIABLE TWINS AND BLIGHTED FETUSES. THE NUMBERS REFER TO THE TWIN BORN FIRST

| TWIN | NUMBER | | PERCENTAGE | |
|--------|-------------|-----------|-------------|-----------|
| | MONOCHORIAL | DICHORIAL | MONOCHORIAL | DICHORIAL |
| Viable | 34 | 72 | 74 | 86 |
| Fetus | 12 | 12 | 26 | 14 |

The data in Table XI seem to show that dichorial viable twins were born before the blighted fetus more often than were monochorial viable twins, but statistical analysis showed that this difference was not statistically significant.

A further analysis of the time at which the viable twin or dead fetus was born showed the following results in the monochorial group: when the viable twin was born first, it was born within 1 to 5 hours before the dead fetus in 33 cases; in only one case was there a delay in birth of the fetus and in this case, it followed the viable birth by three days.⁶⁶ When the fetus was born first, it immediately preceded the viable twin in 11 cases and in only one case was there much time between births and this was only 19 hours.⁵⁴

In the dichorial group however, there was wider variation between the times of birth. In 64 cases, birth of the viable twin immediately preceded the birth of the dead fetus; in one case it was 12 hours sooner⁹⁷; in one case 48 hours sooner¹³¹; in 4 cases, 3 days sooner^{16, 21, 119, 120}; in one case 3 weeks,³³ and in another case 7 weeks elapsed between viable birth and birth of the dead fetus.⁶⁴ In two cases the dead fetus was born on the head of the viable twin.^{84a*, 125}

These analyses indicate that in the monochorial pregnancies, there was less tendency for either fetus or viable twin to be retained in the uterus for an appreciable time after the birth of its twin, than there was in dichorial pregnancies. Such a variation is related to the independence of the placentas in the dichorial pregnancies.

7. *Age of Blighted Twins in Lunar Months in Monochorial and Dichorial Pregnancies.*

In the earlier reported cases, the age of the blighted fetus was estimated from its appearance, and no accurate measurements of length were made. As early as 1834, Francke⁴¹ gave measurements and fol-

*The small letter accompanying a reference number indicates that this is one of several cases described in this particular reference.

lowing that time, the age was estimated from measurements in most reported cases. Finally, with the development of the x-ray, age was determined by judging the degree of ossification. As a result of the early reports, the idea grew that blighting occurred most often from the third to the fifth month of pregnancy in twin pregnancies where one was born viable. According to von Lichem,⁸⁴ such a conclusion is stated in von Winkel's Handbook. Hähnel⁴⁸ in his review of a number of cases, also comes to this conclusion. Peckham-Murray¹⁰⁴ in a review of the literature suggests this opinion and cites as references Settegast, Kieselhausen, and Hohl. Settegast reported a review of 19 cases in which 6 fetuses had died at the third month; 8 at the fourth; 3 at the fifth and 2 at the sixth month. Of 29 cases collected by Kieselhausen, there were 11 fetuses of the fourth month. Hohl reviewed 23 cases of which 13 were fetuses of the fourth month. Unfortunately, I did not have access to these articles. However, these cases probably overlapped each other, and are without doubt included in the cases which I have gathered. The blighted fetuses reported in the literature examined are listed according to chorial character and age in lunar months in Table XII. In those cases where measurements were given, the age in lunar months was calculated by the use of the formula of Seammon and Calkins.¹⁶⁴

TABLE XII. AGE OF BLIGHTED TWINS IN LUNAR MONTHS IN MONOCHORIAL AND DICHORIAL PREGNANCIES. DATA FROM 131 CASES (PERCENTAGE, NEAREST 1.0 PER CENT.)

| CHORIAL CHARACTER | | AGE OF BLIGHTED FETUS IN LUNAR MONTHS | | | | | | TOTALS |
|-------------------|-------------|---------------------------------------|----|----|----|----|---|--------|
| | | 1 | 2 | 3 | 4 | 5 | 6 | |
| Number | Monochorial | 0 | 6 | 13 | 15 | 9 | 3 | 46 |
| | Dichorial | 1 | 9 | 26 | 30 | 15 | 4 | 85 |
| Per cent | Monochorial | 0 | 13 | 28 | 33 | 20 | 7 | |
| | Dichorial | 1 | 11 | 31 | 35 | 18 | 5 | |

Examination of Table XII shows that fetal death occurs to the same relative degree in the same months in both monochorial and dichorial pregnancies. Furthermore, the peak of the highest mortality in both groups is from the third to the fifth months. The greatest number of deaths occurs before the sixth month. As stated above, such a distribution has been suggested by other investigators, but the earlier data have been scattered and not of sufficient magnitude to adequately support this view.

8. *Character of Preservation of the Dead Fetus and Its Relation to the Time of Death in Utero.*

The records of cases examined indicate that the blighted fetus may be physically affected in a number of ways. The variety of change may be briefly classified as follows with regard also to chorial character and incidence of the several types of modification:

I. Nonflattened.

1. Well preserved; monochorial, 3 (6.6 per cent): dichorial, 7 (8.5 per cent).
2. Macerated; monochorial, 2 (4.4 per cent): dichorial, 8 (9.9 per cent).
3. Dried or mummified; monochorial, 2 (4.4 per cent); dichorial, 6 (7.4 per cent).

II. Flattened.

1. Well preserved; monochorial, 23 (51.1 per cent); dichorial, 44 (54.3 per cent).
2. Macerated; monochorial, 4 (8.8 per cent); dichorial, 3 (3.6 per cent).
3. Dried or mummified; monochorial, 11 (24.6 per cent); dichorial, 13 (16.1 per cent).

In the above group, none of the flattened fetuses was putrid, while one of the nonflattened macerated monochorial fetuses was putrid,⁵⁰ and two of the dichorial were so described.^{29, 72}

In addition to the fetuses classified here by chorial character, there were 6 cases in which no chorial character was recorded. Five of these were flattened, of which 3 were well preserved,^{30, 115, 118} one was macerated,¹¹⁴ and one was mummified.⁶⁵

The above brief summary demonstrates that in both monochorial and dichorial pregnancies, the greatest percentage of blighted fetuses which died in utero before the seventh month were flattened (monochorial, 84.5 per cent; dichorial, 74.0 per cent). Those which are flattened and well preserved include also those concerning which no particular remarks were made beyond the statement that they were flat. It is possible that some of these, if they had been examined in detail, would have shown some degree of maceration: The data indicate that chorial character has little to do with the type of modification as there are no significant differences in the distribution of the fetuses in the several categories. Before pursuing the possible factors involved in the modifications, a table showing the relation between the types of modification and the time of death in utero will be given (Table XIII).

Starting with the nonflattened well-preserved class of fetuses, the data in Table XIII demonstrate that this unmodified class is quite widely distributed in the dichorial group, and limited to older fetuses in the monochorial group. Maceration in the nonflattened classes has about the same incidence in both monochorial and dichorial groups, and is confined to fetuses of the fourth month or older. The same distribution is true of nonflattened mummified fetuses.

The flattened well-preserved fetuses form the largest classes in the third through the fifth month in the monochorial group, and in the

TABLE XIII. PHYSICAL CHARACTERISTICS OF BLIGHTED FETUSES OF TWIN PREGNANCIES IN WHICH ONE TWIN SURVIVED. THE LUNAR MONTH OF DEATH OF FETUS, THE TYPE OF MODIFICATION, THE CHORIAL CHARACTER (M IS MONOCHORIAL; D, DICHORIAL) AND THE NUMBER OF FETUSES ARE GIVEN IN SECTION A. IN SECTION B, THE PERCENTAGE INCIDENCE IS GIVEN.

SECTION A. NUMERICAL DISTRIBUTION

| MONTH | NONFLATTENED | | | | | | FLATTENED | | | | | |
|--------|----------------|---|-----------|---|-----|---|----------------|----|-----------|---|-----|----|
| | WELL PRESERVED | | MACERATED | | DRY | | WELL PRESERVED | | MACERATED | | DRY | |
| | M | D | M | D | M | D | M | D | M | D | M | D |
| 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 3 | 0 | 0 | 0 | 0 | 3 | 6 | 0 | 0 | 3 | 3 |
| 3 | 0 | 1 | 0 | 0 | 0 | 0 | 8 | 19 | 2 | 1 | 2 | 3 |
| 4 | 2 | 1 | 1 | 3 | 1 | 3 | 6 | 13 | 2 | 0 | 3 | 5 |
| 5 | 0 | 1 | 1 | 3 | 1 | 3 | 5 | 4 | 0 | 1 | 2 | 0 |
| 6 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 2 | 0 | 1 | 1 | 2 |
| Totals | 3 | 7 | 2 | 8 | 2 | 6 | 23 | 44 | 4 | 3 | 11 | 13 |

SECTION B. PERCENTAGE DISTRIBUTION

| MONTH | NONFLATTENED | | | | | | FLATTENED | | | | | |
|--------|----------------|-----|-----------|-----|-----|-----|----------------|------|-----------|-----|------|------|
| | WELL PRESERVED | | MACERATED | | DRY | | WELL PRESERVED | | MACERATED | | DRY | |
| | M | D | M | D | M | D | M | D | M | D | M | D |
| 1 | 0 | 1.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 3.7 | 0 | 0 | 0 | 0 | 6.8 | 7.4 | 0 | 0 | 6.8 | 3.7 |
| 3 | 0 | 1.2 | 0 | 0 | 0 | 0 | 17.7 | 23.4 | 4.4 | 1.2 | 4.4 | 3.7 |
| 4 | 4.4 | 1.2 | 2.2 | 3.7 | 2.2 | 3.7 | 13.3 | 16.0 | 4.4 | 0 | 6.8 | 6.3 |
| 5 | 0 | 1.2 | 2.2 | 3.7 | 2.2 | 3.7 | 11.1 | 5.0 | 0 | 1.2 | 4.4 | 0 |
| 6 | 2.2 | 0 | 0 | 2.5 | 0 | 0 | 2.2 | 2.5 | 0 | 1.2 | 2.2 | 2.5 |
| Totals | 6.6 | 8.5 | 4.4 | 9.9 | 4.4 | 7.4 | 51.1 | 54.3 | 8.8 | 3.6 | 24.6 | 16.2 |

third and fourth months in the dichorial group, although they are distributed in both groups from the second through the sixth month. These are fetuses classically designated as fetus papyraceus or compressus, terms which as far as I can ascertain, were first applied to the flattened fetus by Settegast (see Peckham-Murray¹⁰⁴) in about 1872. According to Verrier,¹²¹ Paul Dubois coined the term "un petit bon-homme du pain d'épice" or "a little gingerbread man," which was used by the French to designate this type of fetus. Barnes and Barnes¹²⁶ have called this type of fetus, fetus foliaceus.

Flattening and maceration seem to have a higher incidence in the monochorial than in the dichorial group, and also seem to have an earlier trend than when the fetus is nonflattened. Flattening with mummification has a rather wide distribution, but in no month is the incidence higher than flattening alone, so that there must be a specific factor which acts to produce the change by which the fetus becomes dried. It is not the fate of most flattened fetuses. Also mummification seems to have a higher incidence in the monochorial than in the dichorial group.

The physical aspects of blighted fetus as listed here have been known for a long time, particularly that flattening of blighted fetuses occurs most often in the early months of pregnancy. It is referred to by

Guillemeau,^{see 30} Dewees,¹³⁰ Cruveilhier,^{see 117} Playfair,¹⁵⁸ Caseaux and Tarnier,^{see 136} Barnes and Barnes¹³⁶ and others. Quantitative data such as have been presented here, have not been gathered to support this view. Another view which is current and is attributed to Settegast,^{see 104} is that if one fetus dies from the second through the sixth month in a twin pregnancy while its twin survives, the dead twin goes through a hardening or mummification process, but rarely becomes a lithopedion because of the presence of the second fetus. According to von Lichem,⁸⁴ mummification is the typical fate of a fetus which dies in utero from the third to the fifth month of gestation, if its partner survives. The present data do not support this view, as can be seen from Table XIII. The great majority of the fetuses are flattened, but only about a third of those that are flattened become mummified, even though the flattening may occur early in pregnancy. Maceration is generally recognized as occurring in the later months of pregnancy, but these data show that it may occur at any time during pregnancy after the second month.

It is now generally accepted that flattening is not the primary cause of death in all cases, but following death of the fetus, it is flattened by its companion, because the amniotic fluid is absorbed and no more is produced either from the placenta or from the fetus itself. With an idea of testing this view, the cases were examined for reference to the relation between the amniotic fluid and the type of preservation of the fetus. In 25 cases from the monochorial group, some comment was made upon this relation. A brief résumé of these remarks is presented in the following paragraphs.

Two of these cases dealt with a mono-amniotic condition. In one of these, the fluid was normal in amount, and the fetus was well preserved⁷; in the other, the fluid was thick and creamy with a disagreeable odor, and the fetus was flattened and mummified.⁶¹ In three cases where the amnions were separate, fluid was present. In one of these, the fetus was macerated and foul⁵⁰; in the second, the fetus was flattened and well preserved⁴; and in the third, the fluid was coffee-colored and the fetus was flattened.¹² There was one unusual case in which the amnion was well preserved, and a well-preserved fetus was present embedded in a dark brown jelly which contained amniotic bands which compressed the umbilical cord.²³

In eighteen cases, the amnions were separate and there was no fluid in the amniotic cavity. The effects of this condition on the enclosed fetus were not the same in all cases. Two were flat and macerated⁴⁹ as in Case 2 of this report; four were flat and well preserved;^{9, 104, 131, 53} nine were flat and mummified;^{14, 23, 31, 55, 69, 70, 107, 109, 130} one had amniotic bands, and the fetus was flat;⁹⁸ in one, the amnion was fibrous, desquamated, edematous and the fetus was flat and mummified;³ and in one, the amnion was decomposed, but the fetus was flat and mummified.¹⁰³

In brief, these data offer support for the idea that in monochorial pregnancies where one twin is dead, lack of amniotic fluid is followed by flattening and mummification of the dead fetus in only about $\frac{1}{3}$ of the cases. The whole data seem to be against the view that there is a lack of fluid in all cases of fetus papyraceus which become mummified. There is a fairly wide variety of modification, which can occur under conditions in which the amniotic fluid is lacking.

In the dichorial group, there were 42 cases in which some remarks were made concerning the amnion and its fluid. There was only one case in which amniotic fluid was present in normal amount and character, and in this case, the fetus was well preserved.⁸⁰ In one case, there was a normal amount of fluid, but it was creamy and the fetus was flat and mummified;⁹³ and in another, the fluid was green and the fetus was well preserved (Marye, cited by De Marmion²⁹).

In five cases, a little amniotic fluid of unmodified character was present, and in three of these, the fetuses were well preserved;^{30, 57, 67} in one, the fetus was shrivelled, but not flat;⁶⁴ and in another, the fetus was flat.⁸⁸ In two cases, reddish-brown fluid was present in the fetal amniotic cavity, and the fetus in one of these was macerated,¹³ and in the other flat and macerated.¹¹² Aburel² presented 6 cases (3 monochorial and 3 dichorial), five of which had died later than the seventh month, and hence, are not included in this paper, but the cases are of interest because in four of them, the amniotic fluid of the viable twin was chocolate-colored. He thinks that the color has been given to the fluid of the viable by that of the dead twin, and it may be used as a clinical sign of the presence of a dead twin, if such has not been suspected before. In two cases, the fluid was malodorous, and in one of these, the fetus was well preserved;¹²⁴ and in the other, it was flat and macerated.⁷⁸

There were 17 cases in which there was no amniotic fluid, and the fetuses were flattened, but not mummified or macerated.^{17, 19, 23a, 32, 35, 41, 43, 77, 81, 82, 86, 102, 106a and b, 111a, 113, 117, 119} There was one case without fluid in which the fetus was nonflattened, but macerated.⁴⁷ In 9 cases without fluid, the fetus was flat and mummified.^{3, 10, 22, 23b, 25, 91, 108, 113, 127} In two cases without fluid, but in a very early stage of development, no fetuses were found.^{67a and b} In one case, the amnion was deliquescent and putrid, and the fetus was putrid.³²

In four of the above cases, the authors stated that hydramnios was present in the amnion of the viable twin.^{17, 23a, 25, 47} In four cases, the authors said that the marks of compression by the head of the viable twin could readily be observed on the compressed fetus;^{12, 86, 108, 132} and in one case,¹⁰⁹ the viable fetus showed the impression of the fetus on its left frontal bone at birth.

This brief review shows that in twelve dichorial pregnancies with viable and blighted twins in which amniotic fluid was present in the

amnion of the blighted twin, only two of these were flattened. While in 29 cases with no amniotic fluid, 26 of the fetuses were flattened, and 9 of these mummified as well. These data certainly indicate that flattening is concomitant with lack of fluid, but they also deny the proposition that lack of fluid always leads to mummification. The evidence from both monochorial and dichorial pregnancies agrees in this respect.

These data from both monochorial and dichorial pregnancies suggest that with diminution of fluid within the amnion of the blighted fetus, the viable twin as it enlarged, compressed the dead twin by the hydrostatic pressure of its fluid-filled amnion between this amnion and the uterine wall. If the dead twin happens to lie in the region where the viable fetus makes direct contact with the amnion wall, such a dead twin will be flattened more than one which may lie in the region of the placenta on the ventral side, or near the legs of the viable twin. The variations in shape of the blighted fetuses which have been recorded, may I think, be attributed to their position with reference to the head of the dead fetus, rather than to the general pressure of its amniotic fluid.

It is therefore, conceivable that the position of twins in the uterus has something to do with the modification or molding of the body of the dead twin by its mate. Most of the investigators who have examined the characteristics of the flattened fetuses carefully have concluded that most of the pressure has been due to the head of the viable fetus. The data which have been gathered concerning the relative positions of normal twins as they present themselves at birth, and also the data on the presentations of viable twins accompanied by a dead twin may be of aid in explaining the distributions of the modifications of the dead twins which have been observed. It is an open question whether presentation, orientation, and intrauterine orientation are identical in single births, because the single fetus is unhampered in its movements. But in twin pregnancies, it would seem that the presentation would reveal the actual position the twins had in utero, because of the limitations of movement imposed on them after they have reached a certain size, or at about the time the placenta is being formed during the third month. On this assumption, it seems logical to assume that if twins are oriented in the uterus in such a manner that their heads lie adjacent to each other and one of them dies, it is more likely to be compressed than if it were in some other position. The only position in which the dead twin would not be in danger of flattening, is that in which the fetuses are in vertex-breech orientation with reference to each other. In normal twins at birth, such vertex-breech orientation has been recorded in 40 per cent of 536 cases (Ramsbotham¹¹⁰); 34.3 per cent of 1,688 cases (Werth, cited by DeLee¹³⁸); 31.7 per cent of 1,138 cases (Kleinwachter and Reuss, cited by Barnes and Barnes¹³⁶); and 22.8 per cent of 514 cases (Kuder, cited by Stander¹⁶⁷). Thus, on

the average from these data, the position would be favorable for non-flattening in about 32.2 per cent of all twin pregnancies, or in 25 per cent of twin pregnancies in which there is vertex presentations of one of the twins. Data gathered from 77 cases in which one twin had died before the seventh month showed that the viable twin presented cephalically in 92 per cent of the cases. Now, if the proportion of vertex-breech positions were originally the same as in cases where both twins were viable, then 25 per cent of the total vertex presenting cases should have been those in which the vertex-breech orientation was the original position. If this relation as assumed herein is favorable for nonflattening, we should expect that 25 per cent of these 71 cases (92 per cent of the total) should be accompanied by nonflattened twins. Actually 17 of these cases, or 24 per cent showed this condition, one viable and one nonflattened twin. Thus, the data support the original suggestion quite well. On the other hand, the conclusion can be made that in any other position than the above, the fetus is practically always flattened. This conclusion is not only supported by the afore-mentioned data, but by the fact that in six cases in which the viable twin presented in a position other than vertex, the dead twin was flattened.

It is generally held that if a blighted twin dies before the end of the second month, it may completely disappear. Several such cases have been presented by King.⁶⁷ Also, as twins grow in size and one of them dies and is not compressed, the same factors of autolysis which operate to completely destroy younger embryos, will produce maceration without complete disintegration because of the limited time in which autolysis may act. The larger the body, the less chance for complete autolysis so that in the later stages of pregnancy, fetuses which have escaped flattening are, as a rule, macerated.

If the amniotic fluid ceases to be produced and is absorbed and the dead fetus does not lie in the region of the head of its viable twin, then an unflattened, shrivelled, mummified fetus may be produced such as is found in single pregnancies. This is an unusual condition as it is recorded in only 2 monochorial^{54, 69} and 6 dichorial pregnancies.^{26, 25, 36, 64}

Putrefaction, gangrenous character, foulness, etc., are rather unusual in the cases reviewed. Lack of putrefaction is probably caused by the presence of the intact chorion in both monochorial and dichorial pregnancies. If the chorion is broken, then the amnion is exposed to the uterine environment, it is soon destroyed, inflammation occurs and the mass becomes foul and pus accumulates around this foreign body. The cases in which the dead fetus is foul smelling have this common characteristic. Another view which has been suggested by Bianca holds, that if a fetus dies and its chorion is nearer to the air than that of its fellow, it will become infected from organisms which enter through the cervix (cited from Depaul⁷²).

One exception to the general views expressed herein, concerns the fate of the fetus when its twin has hydramnios. Four cases have been noted in the above review. It is conceivable that in such a condition, the formation of the fluid in one amnion at a greater rate than in the other would force the lesser filled amnion with its twin against the uterine wall, and actually kill it by excessive hydrostatic pressure. Szendi¹²⁷ states that hydramnios occurred in 8 per cent of 244 twin pregnancies and was present more often in monochorial, while the incidence in single pregnancies is 0.5 to 1.0 per cent according to Hinselman (see Szendi¹²⁷).

Mummification of the fetus is a puzzling sequence of death. It is a fact that the body becomes dry and hard, but it is difficult to understand how this can take place in the presence of amniotic fluid as reported in several cases.^{26, 28, 36, 64, 69, 79} The only answer which may be given is based on the supposition that the fluid present is secondarily occupying the space around the dead fetus following actual primary disappearance of the amniotic fluid with the subsequent drying of the fetus. This fluid could have come from the amnion of the other twin, or may be fluid which has exuded around the dead fetus from the uterine wall. As pointed out in my description of the fetus in Case 1, the fluid must be a very good preservative when present, because of the manner in which it has maintained the form and characteristics of the minute muscle striation in the heart and the larger ones in the body wall. There is apparently a battle between the enzymes of destruction inherent in the dead body of the retained fetus and the surrounding fluid. The effect of the latter is to fix the tissues in such a condition that as little harm as possible may be done to the viable fetus and the mother. If this effect is fully accomplished, the fetus shrinks and becomes mummified, but if it is only partially effective, certain parts become macerated or completely digested, and the varying degrees of dissolution which have been recorded occur.

In general, it may be briefly concluded that modification of the physical characteristics of a blighted fetus depends on the time at which it dies, its position in the uterus with reference to its viable companion, the amount and character of the amniotic fluid both in its own and in its companion's amnion; and finally whether the chorion is ruptured.

9. Histories of Mothers During Pregnancy.

The clinical data in 139 cases were examined to see what conditions were present in the mother during pregnancy. From the records available, the mothers were classified as: (a) in good health; (b) experiencing acute illness at the time of death of the fetus; (c) having been subjected to external violence or trauma at a time coinciding with the death of the fetus; (d) chronic illness during pregnancy; (e) emotional disturbance coinciding with time of death of fetus; and (f) no history.

TABLE XIV. CLASSIFICATION OF MOTHERS AS TO HEALTH, ACUTE ILLNESS, ETC.; SEX OF VIABLE TWIN AND CHORIAL CHARACTER OF THE PREGNANCY. M, IS MONOCHORIAL; D, DICHORIAL. TOTAL CASES: MONOCHORIAL, 48; DICHORIAL, 91.

A. NUMBER OF INDIVIDUALS IN EACH CLASS

| SEX OF VIABLE TWIN | GOOD HEALTH | | ACUTE ILLNESS | | TRAUMA | | CHRONIC ILLNESS | | EMOTIONAL DISTURBANCE | | NO HISTORY | |
|--------------------|-------------|----|---------------|----|--------|---|-----------------|----|-----------------------|---|------------|----|
| | M | D | M | D | M | D | M | D | M | D | M | D |
| Male | 11 | 13 | 4 | 3 | 0 | 1 | 3 | 5 | 0 | 1 | 1 | 2 |
| Female | 7 | 6 | 0 | 4 | 2 | 1 | 1 | 4 | 0 | 1 | 0 | 1 |
| Sex not given | 1 | 23 | 1 | 4 | 1 | 2 | 1 | 6 | 0 | 0 | 15 | 13 |
| Totals | 19 | 42 | 5 | 11 | 3 | 4 | 5 | 15 | 0 | 2 | 16 | 16 |

B. PERCENTAGE OF INDIVIDUALS IN EACH CLASS

| | | | | | | | | | | | | |
|---------------|------|------|------|------|-----|-----|------|------|---|-----|------|------|
| Male | 23.0 | 14.4 | 8.3 | 3.3 | 0 | 1.1 | 6.2 | 5.5 | 0 | 1.1 | 2.1 | 2.2 |
| Female | 14.6 | 6.6 | 0 | 4.4 | 4.2 | 1.1 | 2.1 | 4.4 | 0 | 1.1 | 0 | 1.1 |
| Sex not given | 2.1 | 25.4 | 2.1 | 4.4 | 2.1 | 2.2 | 2.1 | 6.6 | 0 | 0 | 31.2 | 14.4 |
| Totals | 39.7 | 46.4 | 10.4 | 12.1 | 6.3 | 4.4 | 10.4 | 16.5 | 0 | 2.2 | 33.3 | 17.7 |

From the data in Table XIV, it is evident in both monochorial and dichorial pregnancies where a viable twin is accompanied by a dead fetus, the greatest percentage of mothers showed no subjective symptoms of ill-health. Furthermore, it is probable that in those cases where no history was given, the gestation was so uneventful that it was not even commented upon. Hence, the group of healthy mothers may be even greater than the limited data show. Further examination of the table indicates that the proportion of mothers in good health when the viable fetuses are male is about twice as great as when they are female, in both monochorial and dichorial pregnancies. Such a distribution implies that maleness in either of twins does not necessarily produce more harmful effects on the mother than when they are females. It is possible that in the group classified as in good health, there are mothers who may have systemic disease or organic disease which although not appearing at the time of pregnancy, may affect the health of the fetuses. Such comment is suggested by the recent paper of Miller et al.¹⁵⁶ as a result of their study on the deaths of fetuses of mothers who became diabetic after the pregnancy, which had ended in the death of a child.

In the group of cases included under acute illness which coincided with death of one fetus, physical symptoms such as hemorrhage, escape of amniotic fluid, acute illness, sudden intrauterine pain, etc., were referred to. These symptoms were suggested to be evidence of intrauterine conditions, which in single pregnancies would result in miscarriage or expulsion of the dead fetus and its membranes. Hence, such symptoms are regarded as objective evidence of the time of fetal death. In this group aside from the acute attack, the remainder of the pregnancy was uneventful. In this group there is no significant difference related to chorial character, although in the monochorial group, the cases in which the viable twin is male, are significantly more numer-

ous (8.3 per cent) than in those in which it is female (0 per cent). Hence, the tendency to have acute illness which could be called a missed abortion seems to be more likely to happen in monochorial pregnancies when the viable twin is male.

Trauma to the mother which was coincident with the estimated time of death of the fetus occurred in a small number of cases, monochorial (6.3 per cent), dichorial (4.4 per cent), and undoubtedly caused the death of the fetus. But these cases, however, demand further attention to see whether or not the trauma was merely incidental to a congenital abnormality of the fetus or its membranes. Such an examination of the data is made in the next section.

Chronic illness of the mother throughout pregnancy was present in 10.4 per cent of monochorial pregnancies and 16.5 per cent of the dichorial. Such illness may have been the cause of the death of the fetus, since it was present throughout gestation and did not start at a date coincident with fetal death. Even though there seems to be a higher incidence of illness in the dichorial group, the relative difference between the two groups is not statistically significant. In view of the conclusions of Fournier and Klein,¹⁴¹ from a study of the death of one twin (13 cases) in 210 sets of twins, that syphilis caused the death of most of the fetuses, it might be pointed out here that in the whole group of cases reported here, there were only two cases in which syphilis was reported.^{42, 44} Therefore, it is concluded that since there were only 2 mothers who had syphilis out of 107 cases in which the histories are known, syphilis is not a major factor in the production of blighted twins.

The number of mothers who had an emotional disturbance which they claimed was coincident with the time of death of the fetus is small, and the death of the fetus may not have any relation to this condition. Such a possibility is examined later.

On the whole, the data would seem to imply that the presence of a dead fetus together with its dead fetal membranes has little effect on the mother, since the highest percentage of mothers showed no ill effects, and in those cases where an acute illness occurred coincident with fetal death, the pregnancy continued uneventfully. Therefore, the toxemias of pregnancy, as a general rule, cannot be laid to the presence of degenerating fetuses and fetal membranes. A more extended examination of this question will be taken up in the next section which is concerned with the characteristics of the fetal membranes.

10. *Condition of the Mother During Pregnancy and the Characteristics of the Placenta of the Blighted Fetus.*

The case reports were examined to see what relation there might be between the condition of the mother during pregnancy, and the characteristics of the placenta of the blighted fetus. Much of the data on the placental characteristics were obtained from the older literature,

and are from descriptions based upon the physical characteristics as viewed grossly. The conclusions as to the nature of these characteristics were guided by the prevailing opinion of the nosological meaning of such characteristics. With the introduction of the microscope, a more accurate diagnosis of the morphology of the placenta could be made, and such diagnoses are incorporated in the more recent reports.

The classification of the placentas as given in Table XV is so arranged because of the recurring reference to these larger characteristics. The classes are as follows: (1) placenta in good state of preservation, no gross areas of necrosis; (2) placentas partly preserved, in which there was some evidence of change, but the placental region belonging to the blighted fetus was not completely involved; (3) placentas showing fatty degeneration in which diagnosis has been made largely on color and the physical character of the maternal surface. The placentas looked like fat and felt like fat. In only one case in the older literature, such a conclusion was reached by microscopic examination, which revealed fat droplets in material from the fresh placenta (Wilson¹³⁴). (4) Placentas showing hard atrophy including those cases in which the placenta was described as hard, dense, tough, dried, shrivelled, fibrinous, and sclerotic. In placentas from monochorial pregnancies, such change was limited to the vicinity of attachment of the blighted fetus as in Case 2 of this paper. In some of these cases, the histology of such placentas has been described following microscopic study, but these are very few, and will be referred to in the discussion following the table. Monochorial placentas with vascular anastomoses are not included as such in this table, but will be commented on further in this section.

In addition to the above conditions which have been classified, there were several placentas which were gangrenous or foul, or in which there was extravasation of blood on the fetal surface.

TABLE XV. STATE OF HEALTH OF MOTHER DURING PREGNANCY AND CHARACTER OF PLACENTA. M, MONOCHORIAL; D, DICHORIAL. TOTAL CASES: MONOCHORIAL 15; DICHORIAL, 46. PERCENTAGES GIVEN IN PARENTHESES

| Condition | GOOD PRESERVATION | | PARTLY PRESERVED | | FATTY DEGENERATION | | HARD ATROPHY | |
|-----------------|-------------------|-------|------------------|-------|--------------------|---------|--------------|---------|
| | M | D | M | D | M | D | M | D |
| | No. % | No. % | No. % | No. % | No. % | No. % | No. % | No. % |
| Healthy | 3 (20) | 1 (2) | 1 (7) | - | - | 7 (14) | 5 (33) | 12 (24) |
| Acute illness | - | - | - | 1 (2) | 1 (7) | 3 (6) | 1 (7) | 3 (6) |
| Chronic illness | - | - | 1 (7) | 1 (2) | - | 3 (6) | 2 (13) | 5 (10) |
| Trauma | - | - | - | - | - | 1 (2) | - | 3 (6) |
| No history | 1 (7) | - | - | - | - | 1 (2) | - | 5 (10) |
| Totals | 4 (27) | 1 (2) | 2 (14) | 2 (4) | 1 (7) | 15 (30) | 8 (53) | 28 (56) |

From an examination of Table XV, it can be seen that relatively, the healthy mother in those classes where the history is given, is the

only group in which good or normal preservation has been reported as characteristic of the placenta of the dead fetus. Better preservation is present in monochorial placentas than in dichorial, possibly because the localized necrosis in the former may be compensated by the growth of the normal part of the placenta to such a degree, that grossly, the necrotic region may not be recognized. The same condition could prevail in partially preserved placentas.

"Fatty degeneration" of the placenta seems to be more common in the placentas of dead dichorial twins than in those of monochorial, and has been reported in all of the classes of mothers. Thus, this type of degeneration has no relation to a specific clinical condition of the mother. The term "fatty degeneration" has been used to describe a condition in which the maternal surface of the placenta when viewed grossly, shows yellowish matted masses in the regions where in the normal placenta the cotyledons can be seen. These characteristics have been given in cases where microscopic examination was not made. According to Frankl (cited by Adair¹³⁵), infarcts of placentas resulting from villous degeneration have a yellow color when viewed in the fresh condition. Sarway and Frank (cited from Adair¹³⁵) also define these infarcts as having such a color. Robin and Barns (cited from Adair¹³⁵) seem to be the only ones who suggest that fatty degeneration is coincidental with placental necrosis. From the modern point of view, the cases reported as "fatty degeneration" should be classified as evidences of infarction, which in dichorial placentas include the whole placenta. These represent an early stage in the history of infarction, which is the result of villous necrosis and accumulation of masses of fibrin between the villi (Adair¹³⁵ and Montgomery⁹⁴). These are found normally in senile placentas.¹⁶⁸ Now, if they represent the first stage in the obliteration of the villi which culminates in hard atrophy or dense hard white masses, it would seem that these conditions should be found in those cases in which the fetuses are older than those whose placentas are characterized by hard atrophy. The cases in which hard atrophy were reported are more numerous than those with "fatty degeneration" and it would seem that the great majority of the placentas reach full atrophy during the course of pregnancy. The percentage of hard atrophy is higher in the dichorial group. It is found more often in monochorial than is "fatty degeneration," a difference which may be accounted for by the greater ease with which this condition may be noted in gross examination. If these two types of degeneration are related in point of time, they should show some difference in distribution as regards the time at which the fetus died.

Analysis of the data from 15 cases of "fatty degeneration" and 24 cases of hard atrophy from dichorial pregnancies in which the age of the dead fetus was given, showed no significant difference in distribution of the two types of degeneration with reference to time. In the

fatty group, the time range was from 2.5 through 6.5 months; and in the hard atrophy group, from 2.5 to 6 months. From these distributions, it is concluded that it is not possible to judge from the character of the placenta how long it was in the uterus. Apparently, there is rapid and slow degeneration, and the whole process may not be consummated during the sojourn of the dead placenta in the uterus.

Young¹⁷³ in presenting arguments for an explanation of toxemias of pregnancy states that if the fetus dies and the circulation in the placenta stops and infarction develops, no toxemia will be manifest in the mother. On the other hand, if the placenta becomes partially necrotic, and the fetus remains alive and circulation is maintained in the placenta, toxemia is likely to develop. In all of the cases reviewed here, a viable twin is present together with a dead twin fetus with its necrotic placenta. Yet only a small proportion of individuals containing such twins showed any signs of ill-health even though they contain a viable fetus and a large mass of necrotic material, which according to Young, should induce a high incidence of toxemia. It may be that Young would insist that the circulations of viable and dead placentas are separate, and therefore, the conditions necessary for effect on the mother are not present. Such could be the case in dichorial twins with separate placentas, but in dichorial twins with fused placentas and in monochorial twins in which the necrotic part of the placenta belonging to the dead fetus is intimately associated with that of the viable, the maternal blood circulating in the placenta would certainly be exposed to the conditions suggested by Young as incident to maternal toxemia. In order to test this idea quantitatively, an attempt was made to see how much necrotic placenta could be retained in those cases where the mother was not affected. Unfortunately, in the records of all of the cases examined there were only nine, including Case 1 of this paper, in which measurements of the placenta were given. The data on the volumes of the dead placentas (dichorial pregnancies) showed that these had a range of volume equivalent to from 4.0 to 50.0 per cent of the volume of the viable placenta. Hence, it is concluded that it is possible for the mother to have a large volume of necrotic placenta in the uterus, which even in the presence of a viable twin, produced no demonstrable clinical symptoms as far as can be judged from the reports of the conditions of the mothers in these cases.

Many papers have been written concerning the conclusions as to the cause of necrosis of the placenta as judged from microscopic observations. Adair¹³⁵ has presented an extensive review of the older views on this subject, and other views have been presented recently by McNalley,¹⁵⁶ Montgomery,⁹⁴ Goodall,¹⁴⁴ and Kearn.¹⁵² The problem raised is whether the necrosis of the placenta is caused by primary fetal death, or by primary maternal effective agents. This question has been

attacked by Schultz-Brauns and Schoenholz¹⁶⁵ using the incineration method. According to these investigators, necrosis of the placenta from maternal causes results in a deposition of calcium in the epithelium of the villi; while if necrosis originated with the fetal vascular system, the walls of the vasa of the villi show calcium deposits. They hold that although staining with hematoxylin shows calcium when present in massive amounts, it cannot be adequately demonstrated if present in small amounts. The incineration method does this by removing all of the organic matter and leaving only the metallic ash. The presence of calcium is detected by testing with reagents which reveal the calcium present as gypsum crystals. The study of the placenta of Case 1 of this paper, is the only recent study in which this method has been used. As pointed out in the section on the description of the placenta, the conclusion was reached that the necrosis of the placenta probably had a maternal origin. As controls for this study, the chorionic epithelium and placentas of 51 apparently normal embryos and fetuses from our collection were sectioned and the sections incinerated. In none of these was there any great deposition of calcium in the epithelium, and all of them had only the normal distribution of fibrin in the intervillous spaces, and the epithelium of the villi was normal for the particular stage investigated.

In addition to the conditions of necrosis which accounted for most of the cases wherein a description of the placenta was given, there was one placenta from a monochorial pregnancy in which that part of the placenta belonging to the dead fetus was foul; but in this case, the amnion was ruptured, and no doubt, the condition was the result of bacterial invasion.

Vascular anastomoses in the placenta were, of course, limited to monochorial pregnancies. In the records of 48 monochorial cases examined, there were only 6 reports in which vascular anastomoses were mentioned.^{3, 37, 84, 109, 127, 128} This is quite a small number when it is considered that Schatz (cited by Newman¹⁵⁸) who has studied this condition extensively, concludes that it is one of the primary causes of death of one twin in monochorial pregnancies. Vermelin (cited by Szendi¹²⁷) also supports this view, but Szendi after making an examination of twenty placentas in which vascular anastomosis was present and both twins were viable, considers that it is only a minor cause of death. The present data support Szendi's view. For the manner in which death is brought about in cases of vascular anastomoses, the reader is referred to the excellent discussion in Newman.¹⁵⁸

The description of the dichorial placentas were examined to see if there were any significant differences in the histories of the mothers in regard to the fused or separate condition of these placentas. These data are summarized in Table XVI.

TABLE XVI. DISTRIBUTIONS OF FUSED AND SEPARATE PLACENTAS WITH REFERENCE TO THE CONDITION OF THE MOTHER DURING PREGNANCY—91 CASES OF DICHORIAL PREGNANCY

| TYPE OF PLACENTA | | CONDITION OF MOTHER | | | | | TOTALS |
|------------------|----------|---------------------|---------------|-----------------|--------|------------|--------|
| | | HEALTHY | ACUTE ILLNESS | CHRONIC ILLNESS | TRAUMA | NO HISTORY | |
| Number | Fused | 20 | 8 | 8 | 1 | 4 | 41 |
| | Separate | 22 | 8 | 8 | 5 | 7 | 50 |
| Percent- age | Fused | 50 | 19 | 19 | 2 | 10 | |
| | Separate | 44 | 16 | 16 | 10 | 14 | |

Examination of Table XVI shows that there are no significant differences between the incidences of fused and separate placentas and the condition of the mother, except possibly in the accident group. In this group, it might be possible to conclude that injuries are more harmful and the placenta more liable to injury from trauma if the placentas are separate. If acute illness coinciding with the death of the fetus is produced by an intrauterine condition affecting the placenta, it is apparent that this can affect the fused just as much as the separate placentas, and that fusion of placentas does not offer protection against uterine injury of a subjective nature.

The data were examined to see how frequently miscarriage in previous pregnancies occurred. Out of 150 cases, a history of miscarriage in previous pregnancies was recorded in 7 cases or 4.7 per cent of the total. Although this is a small number in contrast with the whole group, it is, nevertheless, suggestive that in women who have had miscarriages and are undergoing twin gestation, the possibility that one of the twins may be blighted should be borne in mind.

A history of twinning in previous pregnancies was found in 8 cases out of the 150 or in 5.3 per cent of the cases. This is a rather high incidence of a history of twinning in such a small population and would seem to indicate that along with the twinning tendency, there may be changes in the uterus which do not always favor the survival of both twins in those individuals who have already had twins in previous pregnancies.

There were two cases of placenta previa. In one case, the placenta of the viable twin was in this position;⁵⁷ and in the other, the placenta of the dead fetus was abnormally placed.¹³ In the latter case, the viable child and fetus were removed by cesarean section.

11. *Characteristics of the Umbilical Cord.*

A. Monochorial pregnancies. According to Potter and Adair,¹⁶⁶ cord complications or anomalies were mentioned as a possible cause of still-birth in single children in 17.5 per cent of all children who died from known complications in a population of 6,750 stillbirths. The records of the cases discussed in the previous sections were reviewed to find

out, if possible, how many of the dead fetuses of monochorial pregnancies could have had fatal cord complications. Of 21 cases in which the characteristics of the cord were given, only ten showed anatomic evidence of a condition which could have produced death in the fetus by cutting it off from the placenta. These conditions are as follows: cord knotted;⁵ cord looped around the neck and anastomoses of fetal arteries and veins with those of viable in placenta;³⁷ velamentous insertion of the cord with thrombus in the umbilical vein between amnion and placenta;¹⁵ only one artery and vein in both the umbilical cord of the fetus and that of its viable mate with anastomosis of circulations in placenta;¹²⁷ velamentous insertion, anastomoses between viable and dead twin circulations;^{3, 84} velamentous insertion;⁶³ cord cut by amniotic bands.^{45, 98} In one case, the cord was very short and twisted, a condition which could conceivably prevent proper circulation between fetus and placenta.⁷ Of the other conditions of the cord, all could have been secondary to necrosis of the placenta or the fetus, as has been discussed in Case 1. Thus, of 21 cases in which conditions of the cord have been noted, 47 per cent showed complications or anomalies which could have caused the death of the fetus. This proportion of death from cord complications is significantly greater than death from the same kinds of complication in fetuses of single pregnancies. Only three cases of mono-amniotic twins were recorded in the monochorial group. In one of these as noted above, the cord was extremely short;⁷ in the second case, the mother had been exposed to terrific trauma coincident with death of the fetus;⁶¹ and in the third, the cord was marginally attached.¹¹ Thus, in none of these cases was there knotting or intertwining of the cords such as Quigley¹⁶² has reported as a frequent fatal complication of older mono-amniotic twins.

B. Dichorial pregnancies. In this group, no case has been found in which the vasa of the blighted twin were related to those of the viable. This of course, is because of the independent origin and development of the two chorial circulations. Certain characteristics of the cord have been described in 31 cases of dichorial twins, of which one has died before the beginning of the seventh month. Of these, 8 or 26 per cent had modifications of such degree that they could have been the cause of death of the fetus. The conditions described are as follows: (a) wrapped around parts of the body;^{75, 86, 88} (b) compressed by the knees;⁴¹ (c) only one vein and one artery present;¹¹⁷ (d) stenosis of the umbilical vein;²² (e) velamentous insertion;⁸³ (f) separated at umbilicus;²¹ and (g) very short.¹⁰ In the remainder of the cases, the cord was described as normal, atrophied, thin, flat, soft, hard, etc. All of these modifications could have been secondary to necrosis of the placenta as I have shown from a study of the cord of the fetus in Case 1 of this paper. Thus, the percentage of death of fetuses in dichorial pregnancies from cord complications is greater than in single pregnancies, but less than in monochorial pregnancies.

In comparing the monochorial and dichorial pregnancies with regard to umbilical cord complications, it is of interest to note that there were five cases of velamentous insertion in the monochorial group, and only one in the dichorial group. According to Williams,¹⁶⁸ velamentous insertion occurred in 1.25 per cent of single pregnancies; and he cites Lefevre as having found an incidence of 0.84 per cent velamentous insertions in 15,891 cases of single placentas, and Miranoff as recording an incidence of 0.57 per cent in single placentas, but of 5.0 per cent in twin placentas. The present data would seem to supplement this view as regards twins, with the corollary, that velamentous insertion is more common in monochorial than in dichorial twins. In view of the origin of this condition as a result of shifting of the placental blood plexus, it is not surprising that it would be found more often in placentas of twins derived from a single ovum than in those derived from two independent ova.

Summary

An attempt has been made to bring together as much information as was available in the literature concerning the maternal history and fetal relations in twin pregnancies in which one twin was born viable at or near term together with a blighted twin which had died in utero prior to the beginning of the seventh month of pregnancy. Two cases of this kind available to the author have been included and used as a basis for an analysis of the cases reported in the literature. One hundred and fifty cases have been used for the presentation of the comparative data. Also data on normal twinning, placentation etc., have been used as supplementary material.

Some of the more important results may be briefly summarized as follows: Blighting occurs in the same proportion in monochorial as in dichorial pregnancies; it occurs more often in primiparas when the pregnancy is monochorial. There is greater degree of blighting in dichorial pregnancies when the mother is 30 to 35 years of age or over forty years of age, than at any other time either in dichorial or monochorial pregnancies. There is no sex bias in blighting. Surviving twins are heavier than either of twins of viable twin pregnancies.

The viable twin is usually the first born, and is usually presented in the cephalic position.

The greatest incidence of blighting is from the third through the fifth month; flattening of the blighted twin is its usual fate, but it may remain well preserved, nonflattened, macerated or mummified. Amniotic fluid is usually lacking in amniotic cavities of fetuses which are flattened and mummified, but fluid of unknown origin may be present around a mummy which is hard. The position of the fetus in the uterus prior to death is suggested as being related to the kind of physical modification which it undergoes. Hydramnios may be a factor in flattening, but it is not the only factor.

An uneventful course of pregnancy is the rule rather than the exception. Syphilis occurred in only two reported cases.

Detailed histologic study has revealed the remarkable preservation of muscle striations in the heart and voluntary muscle of a 4.9 month fetus papyraceus, which was retained in the uterus with its viable twin until term.

Varying degrees of preservation were reported for the placentas. They were practically always necrotic either in part (monochorial), or in whole (dichorial). The incineration method was applied to sections of the placenta of the 4.9 month fetus (Case 1), and it was revealed that calcium deposits were confined to the original sites of the chorionic epithelium, a condition which Schultz-Brauns and Schoenholz hold is evidence for the primary necrosis of the placenta as of maternal origin.

Vascular anastomoses in the placentas of monochorial twins have been recorded as occurring in only a few cases of blighted twins, so that it is considered not to be a great factor in the death of one of monochorial twins.

Cord complications which could lead to death of the fetus have been recorded in relatively more cases than is characteristic of single pregnancies. The characteristics of the umbilical cord in Case 1 of this paper, show that necrosis progressed from the placenta toward the fetus.

Uniformity of recording the characteristics of blighted fetuses is suggested as a valuable aid in extending our knowledge of this condition, since we cannot set up experiments in animals which will parallel the conditions peculiar to human plural gestation.

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THE CONDUCT OF THE THIRD STAGE OF LABOR

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IN 1939 Leff¹ stated after an experience of 7,500 personally conducted labors that the third stage of labor, "consists of two phases; the first, the separation of the placenta; and, the second, the delivery of the placenta. The separation of the placenta is a normal physiologic process which is accomplished entirely by the contractions of the uterus and the reduction in its size as soon as the baby is born, while the second phase, the delivery of the placenta is, as a rule, not accomplished by the natural forces, but must have the assistance of the obstetrician. . . . The delivery of the placenta has to be aided artificially." Previously, Warnekros² in 1918, and Weibel,³ independently in 1919, demonstrated by x-ray studies that the placenta separated within five minutes after the delivery of the baby, and that one or two postpartum contractions sufficed to accomplish this separation. They showed also that there is little evidence of the retroplacental hemorrhage or hematoma still illustrated by imaginative drawings in textbooks. Weibel³ found in some cases where it took only one to one and a half minutes to take the first x-ray picture after the delivery of the baby, that the placenta was already separated by the time the dye was injected. Recently, Danforth, Graham, and Ivy⁴ by sagittal sections in monkeys concluded that separation of the placenta is almost complete by the end of the second stage of labor in these animals and, by analogy, felt that this was probably true of human beings. Titus⁵ from a sagittal section study of a woman who died at the end of the second stage concluded that the placenta in this patient was sheared off by the uterine contractions without any retroplacental bleeding. Greenhill,¹⁰ Davis,⁶ Boynton,⁶ and others have come to the same conclusions.

Leff¹ stated that "the generally considered signs of separation of the placenta" (i.e., descent of the cord, rising up and change in shape of the uterus, and bleeding) "are of no value. There are no signs. The placenta separates immediately." As regards the effect of narcotics or anesthetics on the mechanism of separation, the majority of observers feel that these slow the mechanism somewhat. In my experience, the separation is occasionally not complete because of the effect of anesthetics or large amounts of analgesics. However, intravenous ergotrate compensates for this deleterious effect of analgesics and anesthetics. Thus Davis and Boynton⁶ in 1,000 patients found that the placenta not only separated, but was actually delivered in less than three minutes when intravenous ergotrate was given with the delivery of the shoulders.

In common with all who have used ergonovine intravenously, they feel that its use promotes and hastens this normal, natural, quick mechanism. The signs mentioned above are those of expulsion of the placenta into the lower uterine segment or vagina, and not signs of separation of the placenta from the wall of the uterus. The signs vary greatly in the time of their appearance and, indeed, may never appear. The last mentioned viz. bleeding, I consider pathologic because it indicates partial retention of blood in the uterus behind an *already separated* placenta which is not being expelled from the uterus. Conditions are proper for the delivery of the placenta within one minute after the intravenous injection of ergotrate, and in the unanesthetized woman within one or two minutes after the delivery of the baby even without the use of this drug. From our knowledge of the physiology of this stage, I believe that we should terminate it promptly. Such is not the common practice and teaching, however. This is due possibly to a misunderstanding of the mechanism of the third stage. Thus Rushmore⁷ in 1937, asked in the Massachusetts State Board Examinations, "Give in detail your treatment of a patient in whom there appears no sign of separation of the placenta twenty minutes after the birth of the child." He says, "It is hardly necessary to note that this is a perfectly normal case as described although there is a possibility of complication arising." In view of the opinions already expressed, I believe that he is confusing separation of the placenta with its expulsion into the lower segment. The case is not normal if the placenta has not separated at the end of twenty minutes. He calls this a "simple question" and "easy answer." I consider it neither. Of 250 candidates, 182 failed to pass on this question. The answers were varied in the extreme. Failure to terminate the third stage of labor quickly, results in the retention of the placenta many times. Jellet⁸ states that such a retention "is one of the most common complications of labor . . . and in some cases the placenta would be retained in utero indefinitely." Moreover, this retention either with or without a later hemorrhage not infrequently requires its manual removal. Thus at the Rotunda previous to 1929 in 45,000 deliveries with a cautious policy of noninterference with this stage of labor, and in women not usually narcotized nor anesthetized, the incidence was one in 75 cases. More recent statistics, those of Schwartz and Richards,⁹ reveal retention once in every 120 deliveries. Moreover, more women die in this stage of labor than in any other, due it is true generally, to pathology of pregnancy, or of the first or second stages of labor, but due also sometimes to an inherent risk in this stage even in normal women with normal deliveries of their babies. I believe that a change of viewpoint as to the mechanism of the third stage of labor and a resulting change in management of this stage will lessen this inherent risk.

At the present time, most obstetricians recommend simple placing of the hand on the uterus, and when the uterus rises into the abdomen

and the cord slips farther out of the vagina, to then express the placenta from the cervix or vagina by a downward and backward push without squeezing the uterus as is done in true Credé technique. I repeat, however, that the signs mentioned in the various texts are those not of separation of the placenta, but of the presence of the placenta in the lower segment of the uterus, the cervical canal, or the vagina, and one may wait a long, long time for these phenomena to appear with the ever-present danger of the uterus filling up with blood or, on the contrary, contracting so firmly about the placenta as to imprison it. A brief consideration of the leading texts will show that the distinction between separation of the placenta and expulsion of the placenta from the uterus, a distinction fundamental in the proper treatment of the third stage of labor, is not clearly stated. Thus Beck¹⁰ teaches to wait until the fundus rises and the cord protrudes or slips down and there is a gush of blood, all of which he says, "show conclusively that separation of the placenta is complete." But the separation is complete long before this. He does not allow expression of the placenta until these signs appear. After an hour, he consents to a "true Credé." He believes it unwise to leave the placenta within the uterine cavity for more than three or four hours, since its separation may at any time be accompanied by a profuse hemorrhage. This is in complete disagreement with Schumann¹¹ who allows the placenta to stay within the uterus for twenty-four hours. It seems to me, moreover, that if it is unwise to leave the placenta in for three hours, it is unwise to have it in the uterus at the end of four hours. Stander¹² waits at least an hour before manual removal, unless bleeding occurs. One "should not despair" and should "try repeated Credé" even though many men condemn repeated Credé as too bruising, shocking, and unsurgical Titus⁵ recommends several attempts at Credé for at least two hours, and then says that "manual removal must be considered." Greenhill¹³ believes it is "safe to wait up to twenty-four hours as almost always nature will expel it" but Williams¹⁴ long ago pointed out that "should the placenta be allowed to remain in the uterus, someone qualified to remove it manually should be in constant attendance." DeLee¹⁵ believes one may safely wait, not one, two, three, nor four nor twenty-four hours, but eight or ten hours, although he states that after one hour the third stage is pathologic and Credé should be done. If at the end of an hour the condition has become pathologic, why procrastinate? Calkins,¹⁶ moreover, points out that "expulsion of the placenta into the lower segment or vagina occurs spontaneously in only a small percentage of patients. The attendant should, therefore, express or aid the patient to expel the placenta." He found that of 1,577 cases, the placenta separated in 69 per cent in less than five minutes. He goes on to say that "this is in sharp contrast to our older ideas of 15, 20, or 30 minutes for the duration of the third stage." The cautious attitude expressed by

many writers is due chiefly to the fear of invading the uterine cavity and thereby producing sepsis. Williams¹⁴ insisted that it was dangerous to invade the uterine cavity. Jellet⁸ alone feels that the risk of manual removal "is very small, indeed" if only we "wear rubber gloves," a request with which it certainly is not too difficult to comply. In addition, certain of these disagreements, and the cautious attitudes to be found in modern texts are due to the tradition that the expulsion of the placenta is an easy, natural, normal process and the rule. I do not believe that this is true in the narcotized, anesthetized patient. I believe, too, that the traditional hands-off policy is due to teachings directed at the lowest possible levels of skill, or rather lack of skill, in the profession. On the contrary, Ricci and Marr¹⁷ believe that "obstetrics is a surgical and not a medical specialty" and that the obstetrician should "absorb the gynecologist's surgical skill in the pelvis" and "his appreciation of the structure and function of the soft parts of the vaginal canal." It is not surprising that infection after manual removal of the placenta is comparatively common if the operation is not performed until long after delivery when bacteria have invaded the uterus; until after many brutal attempts at Credé have been practiced; until after the patient has lost too much blood. After three hours the uterine cavity is loaded with bacteria, according to Leff.¹ Prolonged anesthesia is not good for a patient. All writers point out the danger of continuous or intermittent losses of small amounts of blood, a state of affairs which frequently results when one waits indefinitely for the completion of the third stage of labor.

The technique followed here is not new. In fact, in some ways it is a reversion to the practice of immediate removal of the placenta, manually if necessary, so common in the middle of the nineteenth century. The procedure advocated here has been used on 900 private patients with good results. The principles underlying this procedure will be briefly stated; then the steps outlined and the results given. The bases of the management and treatment here advocated are: 1. A belief that the placenta separates rapidly. 2. The belief that analgesics and anesthetics tend to interfere occasionally with a complete separation and tend to delay this rapid and complete separation, but that ergonovine intravenously with the delivery of the child will restore this normal mechanism. 3. The belief that the anesthetized patient will not expel the placenta but that simple, safe, surgical procedures will.

Procedure: 1. As soon as the baby's anterior shoulder is delivered, one ampule of ergonovine is given intravenously and the cord is clamped and cut. (Twins must be ruled out, and for this reason I do not feel that the use of intravenous ergotrate is safe in clinic practice.) 2. The clamp on the placental end of the cord is released and what blood is left in the cord and placenta is allowed to flow out thereby reducing the bulk of the placenta. (If the baby is not narcotized and there is no

hurry in its resuscitation, most of this blood can be milked into the baby with benefit to the latter.) 3. The hand is placed on the fundus. If the ergonovine has been timed properly, the uterus will have contracted vigorously and the already separated placenta is expressed into the vagina and then into the basin. If there has been a delay in the administration of the ergonovine or a rather deep anesthesia has been given, it may be necessary to wait for the very vigorous contraction that the ergonovine causes. Expression is then performed. If the placenta does not come into the vagina, a minute is allowed to elapse and then pressure is repeated. If it is not expelled with this maneuver, the cord is pulled upon, always with one hand on the fundus to make sure that the uterus is hard. DeLee¹⁵ condemned this practice, but admitted that it is "not dangerous in skilled hands." Over 90 per cent of my patients are delivered by the first two, and if necessary the third maneuver, within three or four minutes. 4. Should the placenta still be present in the uterus, the cervix is examined and if the membranes are found across the internal os, following Leff's¹ recommendation, the finger (or a snap) is passed at the side of the cervix. Frequently, a fair amount of blood escapes and the placenta is then expressed by fundal pressure. 5. Should the placenta still be in the uterus, the old recommendation of Edgar¹⁸ made in 1903, is followed. He stated that when the placenta was adherent and Credé failed, he found that if he passed a few fingers through the cervix, that he could grasp the lower end of the placenta and with the outer hand on the fundus to insure a firm uterus, the placenta could be readily drawn from the uterine cavity. I find it necessary to do this in about 6 per cent of the patients. 6. In about one case in 60, I find that these maneuvers are not enough and thereupon change gloves, use antiseptics freely, and pass my hand into the uterus, finding usually a firmly contracted uterus holding an already separated placenta. The placenta is firmly grasped and withdrawn. Occasionally, I find that the placenta is not completely separated. I remove the placenta about one-half as often again as in the statistics given by Jellet,⁸ and about twice as often as shown by the recent statistics of Schwartz.⁹ I believe that the increased frequency is more than compensated for by the fact that it is done before the patient has lost blood, and before the uterus contains bacteria. Moreover, I feel that the dangers of manual removal of the placenta have been overemphasized. I think that many obstetricians today conduct the third stage of labor in the manner outlined up to the point of manual removal but then wait if the previous maneuvers have failed. Thus, Greenhill¹⁹ advises waiting until the effects of the ergonovine wear off, if the placenta has not separated. 7. After the placenta is out, the uterus is anteflexed over two fingers passed against the anterior lower segment following the recommendation of Leff,¹ and the uterus vigorously massaged removing any clots or liquid blood.

Results: There have been 900 private patients delivered through the vaginal canal. The maternal morbidity has been insignificant.

| | Number | Percentage |
|--------------------------------------|--------|------------|
| (1) Puerperal sepsis | | |
| (a) Phlebitis | 1 | 0.11 |
| (2) Postpartum hemorrhage | 8 | 0.88 |
| (a) Due to cervical lacerations | 4 | 0.44 |
| (b) Due to inertia | 2 | 0.22 |
| (c) Due to retained placental tissue | 2 | 0.22 |
| (3) Maternal mortality | 0 | |

The case of puerperal sepsis was one of phlebitis. This patient had a normal quick delivery of the placenta without bleeding. The postpartum course was uneventful. Phlebitis developed on the fifteenth day, two days after the patient was home. Of the eight cases of postpartum hemorrhage, four were due to cervical lacerations requiring sutures and due, therefore, to the method of delivery or mechanism of the second stage, and not to the conduct of the third stage. Of the remaining four cases; two were cases of delayed postpartum hemorrhage both with normal delivery of the placenta. One of the patients had twins, and the uterus was allowed to fill up three to five hours post partum. The other patient also had a secondary hemorrhage about two hours post partum, and required packing as did the first patient. Two other patients had bleeding after they were home, required a curettage because of excessive bleeding, and revealed small pieces of placental tissue. Both of these patients had the placenta removed by pressure on the uterus with the finger through the cervix without the admission of the whole hand into the uterus. Undoubtedly, a small part of the placenta had not completely separated in these patients and examination did not reveal the defect. Probably the examination of the placenta was too cursory. In one other patient in this series, a defect was found in the placenta and placental tissue was immediately removed from the lower part of the uterus. No cases of contraction of the cervix have been noted.

Summary and Conclusions

1. The available clinical and experimental evidence indicates that the placenta separates from the uterus immediately at the end of the second stage of labor, or within one or two postpartum contractions.

2. General anesthetics and large doses of sedatives tend to delay the speed of this mechanism and in some cases interfere with the completeness of it, but ergotrate intravenously following the delivery of the child tends to restore the mechanism to normal.

3. Separation of the placenta from the uterine wall and expulsion of the placenta into the lower uterine segment or through the cervix are different processes. The first is accompanied by no signs, whereas, the second is accompanied by a rising up of the uterus, the descent of the cord, and sometimes bleeding.

4. The distinction between these two processes is not always clearly maintained, and this accounts in part, for the contradictory advice found in modern texts as regards the conduct of the third stage of labor.

5. The bases for the procedure here advocated are given, the steps of the procedure are detailed, and the results in 900 consecutive vaginal

deliveries in private patients are stated. This active form of treatment which terminates the third stage of labor within five to seven minutes is believed to give excellent results.

The writer wishes to express his appreciation to Charles J. Kickham, M.D., Chief of the Obstetrical Service of St. Elizabeth's Hospital, Boston, Mass.

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CYCLIC OVARIAN CHANGES IN ARTIFICIAL VAGINAL MUCOSA

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THIS case demonstrates the finding of cyclic ovarian changes in the mucous membrane of an artificially-produced vagina, in a girl presenting a congenital absence of uterus, vagina and hymen. These changes have been found by examining the cells desquamated using the vaginal smear method of study. This artificial membrane was induced to grow up from the vulval mucous membrane below. Vaginal smear studies taken daily over a period of two months show the normal variations of the morphology of the squamous epithelial cells, found in the follicular (regenerative) phase and in the luteal (secretory) phase, and it is possible to estimate approximately when ovulation occurs, and when menstruation would occur. They show further, a normal fluctuation of the cornification count from week to week, the cornification curve representing variation in the estrin level showing a cyclic rise and fall during a month, which would appear to be within normal limits.

In order to reveal the true significance of these findings, it would perhaps be best to describe briefly the technique used in producing the new vagina.

The patient was a girl of 18 years who presented herself with a history of amenorrhea. Inspection revealed an attractive girl with apparently normal secondary sex characteristics. Pelvic examination showed normally developed labia and urethra, but no trace of any vagina or hymen. Rectally, no uterus or other pelvic organs were palpable. Closer examination showed normal physical development in all other respects. The breasts were somewhat smaller than average, and pubic hair was not profuse in quality, resembling the picture of a girl who had just reached puberty.

Method.—The patient was hospitalized, and under anesthesia, an opening was made between the bladder and rectum to admit one finger. No further penetration was attempted at this time because of the extremely thin membrane between the rectum and bladder. The new passage was devoid of any epithelial lining, and in an effort to keep it open, a wax mold (dental wax) was inserted, lubricated with sulfathiazole paste.

The patient was allowed to leave the hospital in a few days, the obturator held in place comfortably by a common menstrual belt and pad. She was seen each week, and the mold removed, the cavity cleaned out, and the marginal rim of the vulval mucous membrane was cauterized with 20 per cent silver nitrate. On each visit, it was observed

that the squamous epithelial zone had crept a little higher up the canal forming a sleeve around the obturator. This gradual upgrowth was enhanced further by the fact that the mold was allowed to protrude about one inch below the vulva, and the patient was advised to sit on



Fig. 1.—Showing external genitalia and digital examination of artificial vagina.



Fig. 2.—Showing two dilators (wax molds) worn successively in the process of deepening and epithelization of vagina.

this in such a way as to produce constant upward pressure. At the end of six weeks, the patient was readmitted to the hospital for a few days, and under sodium pentothal anesthesia, the passage was dilated and deepened and a larger obturator was inserted.

This procedure was repeated at one- to two-month intervals, four separate sizes of obturator being used successively. It is noteworthy that throughout this period the patient was ambulatory, no major operative procedure was necessary and she was able to continue her work except for a three- or four-day period following each admission.

Vaginal smears were taken at intervals from the squamous zone, and the cells desquamated exhibited a variable degree of cornification at an early stage indicating the presence of estrin. This finding confirmed ovarian secretion even before it was known for certain that the ovaries were present.

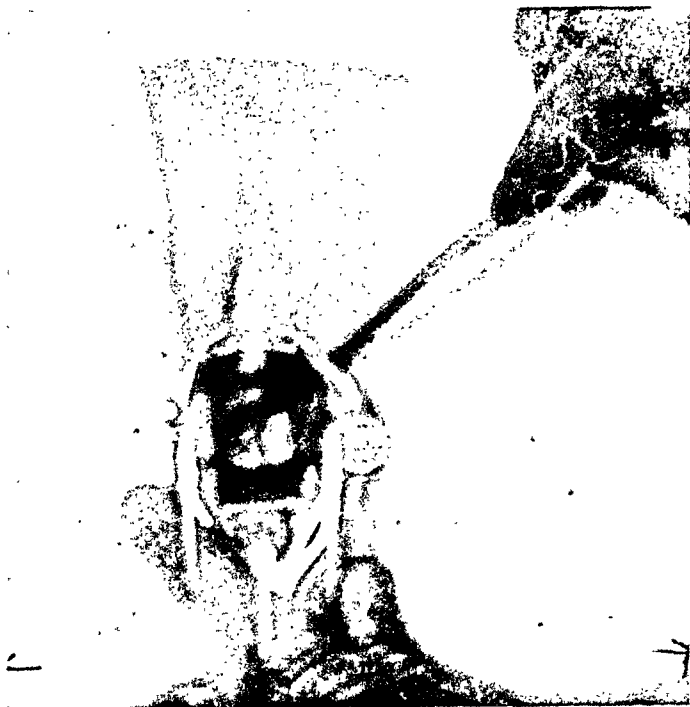


Fig. 2.—Speculum examination showing capaciousness of new tract. Small granulating spot persists at top of vault at this time.

As a sleeve of squamous epithelium gradually grew higher up the canal, the area of granulation tissue diminished. At no time was there difficulty encountered with bleeding, infection or toxic absorption from this raw area.

Six months from the initial operation epithelization of the new vagina appeared complete. At present the passage accommodates the large obturator shown (Fig. 2), which measures 5 inches by $1\frac{1}{2}$ inches (diameter). When the mold is removed, the epithelium contracts slightly presenting the same corrugated appearance as the normal vagina. Indeed, the new tissue resembles closely vaginal epithelium in all respects and pelvic examination reveals similar findings to what one would expect in a woman who has had a total hysterectomy. The ovaries are readily palpable. Following completion of the vaginal passageway, an attack of acute appendicitis permitted a laparotomy

at which time it was possible to take photographs of the pelvic floor. The findings were quite interesting. The ovaries and rudimentary tubes were present, but there was no uterus and the pelvic floor was perfectly smooth. Extending caudally from the region of the ovaries were two cord-like structures of muscular appearance which terminated blindly in a bulbous nodule on each side just two inches caudal to the ovaries. A few strands of tissue of the same appearance passed on down to merge with the flat pelvic floor. The interpretation is that the nodules are the anlage of the Müllerian ducts which failed to descend sufficiently to unite in the midline to form the uterus and vagina, while the strands of tissue which reached the pelvic floor are the rudiments of the ducts of Gartner.



Fig. 4.—Abdominal laparotomy, tenaculum holds ovarv. Note absence of uterus. Pelvic floor is flat except for ridge between bladder and colon.

Clinically, at the present time the vagina would appear to be of normal dimensions, but it is still necessary to wear the obturator intermittently to prevent shrinkage. This has been observed to occur slowly if the mold is left out many days in succession. There is no muscle wall in this new vagina to help it maintain its tone, and capaciousness. The patient is at present engaged and hopes to marry in the near future, the prospects of infertility having been clearly outlined to the fiancé. Probably following marriage the obturator will not need to be used so frequently.

Vaginal Cytology.—Vaginal smear studies were made following the completion of squamous epithelization. The results revealed that the new mucosa is desquamating, reacting to the ovarian hormones in a similar manner to the normal vagina. Daily smears were prepared in our Department of Vaginal Cytology, interpreting the cyclic changes as described by Papanicolaou¹ and De Allende, Shorr and Hartman.² In our laboratory, we have worked out a technique of doing a cornification count comparable to a blood count. The number of cornified cells present out of a total of one hundred epithelial cells counted, gives the percentage. This, it is felt represents fairly accurately (when done by

~ CORNIFICATION CURVE IN ARTIFICIAL VAGINA ~

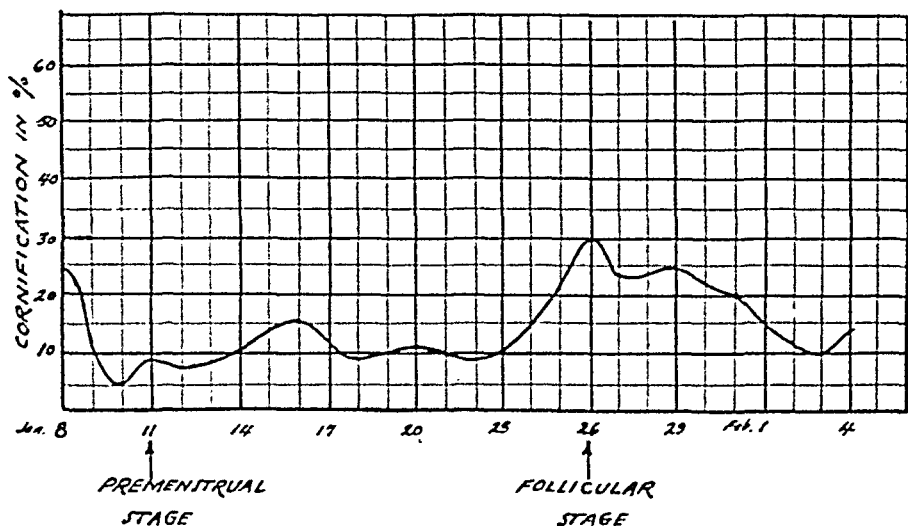


Fig. 5.—Showing cornification curve. Arrows show time of smear (below) illustrating two stages.

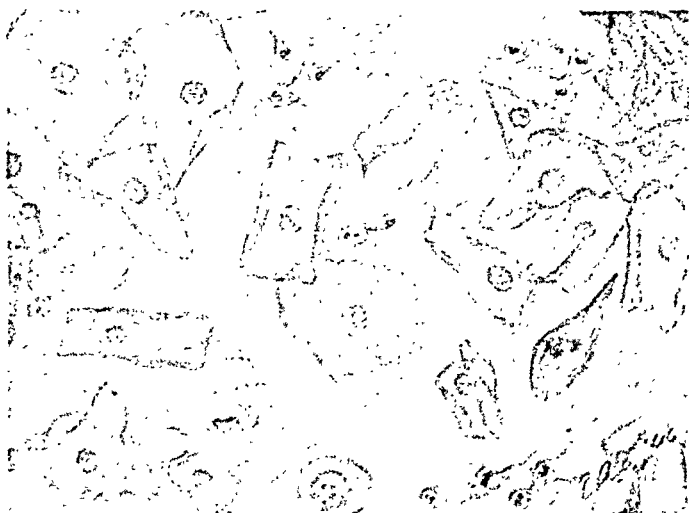


Fig. 6.—Showing premenstrual (luteal) phase. Note folding and clumping of cells which stained basophilic.

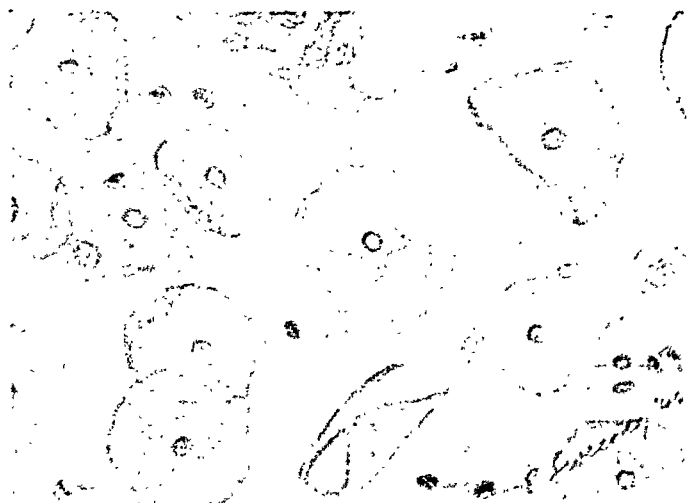


Fig. 7.—Showing follicular stage. Many of the large water-shaped cells are cornified or pre-cornified. Tiny cells are leucocytes from granulating spot in vaginal vault (present in both phases).

a standard routine) the quantitative level of estrin at that particular time. Daily cornification counts over a period of several weeks when charted on a graph give a cornification curve which will show the ebb and flow of the secretion of this hormone. (Fig. 5.) In this case plotting the cornification counts reveals a cyclic trend as shown. Study of the smears from week to week has revealed two different phases which seem to correspond to the regenerative or follicular (Fig. 7), and the secretory or luteal (Fig. 6). Note that in the follicular phase the cells are more discrete, the cornified cells are large and wafer-shaped with a small deep-staining nucleus. The cornification count is highest during this phase and many precornified cells and cells of the estrogenic superficial series are also present. In the luteal phase (Fig. 6), the cells show more folding and shrinkage, there is well-marked clumping of epithelial cells, the cornified cells diminish and the basophilic-staining estrin withdrawal and luteal superficial cells become more prominent. (Fig. 7.)

It would appear from the smear studies that while there is evidence of cyclic changes, the degree of ovarian activity in so far as estrin-secretion is concerned, is on the low side of normal. Many normals show a cornification level up to 60 per cent or 100 per cent. The highest level reached during the cycles under investigation was 40 per cent.

From the cornification curve and the finding of the two phases, the approximate time of ovulation and of menstruation may be postulated. That ovulation is occurring cannot be said with absolute certainty, but there would appear to be presumptive evidence of this phenomenon.

It has been stated that only tissues derived from the Müllerian ducts respond to the ovarian secretions. In this case, the vaginal tube definitely had no Müllerian origin, as it grew up from the vulva under our eyes. Yet, in its new environment, it is very definitely reacting to the ovarian secretions. It would appear that the same cyclic phenomena occur in the vulval squamous epithelium.

Summary

A case of congenital absence of uterus, vagina and hymen has been presented with a simple method of producing a satisfactory artificial vagina without resort to major surgery, while the patient may be kept ambulatory.

Cyclic ovarian changes have been demonstrated in the artificial vaginal mucosa with differentiation of the two phases (follicular and luteal) in the vaginal smears. A cornification curve representing the variable quantitative level of estrin secretion would appear to follow the approximate anticipated pattern in accord with the cyclic phases. The approximate times of ovulation and menstruation have been hypothesized.

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LYMPHOGRANULOMA VENEREUM IN PREGNANCY

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LYMPHOGRANULOMA venereum is a disease of many aliases—lymphopathia venereum, lymphogranuloma inguinale and Nicolas-Favre disease. This last name has special reference to the type associated with inguinal adenopathy which was described in 1913, by Nicolas and Favre. In 1928, Frei first demonstrated that the skin test which bears his name, was frequently associated with stricture of the rectum. Two years later, in 1930, Hellerstrom and Wassen isolated the virus which causes this disease and transmitted it to monkeys by intracerebral injection. The past decade has witnessed the transmission of the disease to a host of other animals, the use of complement fixation tests and the development of a mouse-brain antigen for skin testing.

Lymphogranuloma is caused by a virus which is about the same size as the virus of smallpox—0.1 to 0.2 microns. The virus readily passes through a No. 5 Berkefeld filter. Cytoplasmic granules which are seen in the exudate, are believed to be due to the virus.

There is an apparent increase in the incidence of the disease, but this may be due to increased recognition. There were, during the years 1934 to 1940, according to Grace, 35 patients with lymphogranuloma venereum admitted annually to the New York Hospital. This constitutes 0.1 per cent of the total admissions.

The disease begins insidiously. After an incubation period of 2 to 3 weeks, a primary lesion develops. This may be either an ulcer or an herpetiform lesion. It is located on the vaginal or rectal mucosa, or on the surrounding perineal skin. Because of its innocuous character and transient nature, it is rarely seen. During the next 10 to 50 days, systemic involvement occurs. The Frei test which like the tuberculin test merely indicates sensitivity, then becomes positive and remains so for life.

There are three main types of lymphogranuloma venereum—the anorectal which is the largest group, comprising 60 per cent of the cases, the inguinal which accounts for 25 per cent of the cases, and lastly the genital type which consists of only 10 per cent of the cases.

TYPES OF INVOLVEMENT

| | |
|---------------|-----|
| Anorectal | 60% |
| Inguinal | 25% |
| Genital | 10% |
| Miscellaneous | 5% |

In the male, the primary lesion is usually on the penis. Because of the lymphatic drainage the inguinal glands are involved, while anorectal involvement is less common in the male. In the female, however, the inguinal nodes are rarely affected; genital and anorectal localization being more common. In the inguinal type, there are indurated inguinal nodes, which later suppurate, leaving draining sinuses. It is a clinical observation that patients with inguinal adenitis rarely have anorectal infection. During this period, there may be systemic symptoms—such as fever which is remittent in type, headache, malaise and arthritic pains. The genital type is either an ulcerative lesion (the so-called esthiomene), or else shows the late changes of lymph stasis and fibrosis which result in elephantiasis. Incidentally, an indolent vulvovaginal ulcer is the most infectious variety of lymphogranuloma venereum. By far the greatest percentage of patients with lymphogranuloma venereum has anorectal involvement. This is especially true of women. In the early stages, there is a proctitis manifested by bloody, purulent discharge from the rectum. In the later stages, there is stricture formation which results in increasing constipation and a decrease in the diameter of the stool. These strictures are usually single, but may be multiple. They are either annular or barrel-like, and may obstruct from 1 to 10 centimeters of the rectal mucosa. Frequently, it is not the fibrosis of the strictured area which causes the obstruction, but the superimposed edema from lymphatic and venous stasis. Other rare types of lymphogranuloma venereum include edema of the eyelids and stricture of the urethra.

LOCALIZATION

EARLY
Primary lesion
Inguinal adenitis
Proctitis

LATE
Rectal stricture
Elephantiasis of the vulva

When any of the above symptoms and signs are present, the diagnosis is readily made by the Frei test. This consists in the intradermal inoculation of an emulsion containing inactivated virus. Depending upon its source, the virus is known as human, mouse brain or chick embryo. When the test is read in 48 to 72 hours, an erythematous area, which is over 6 mm. in diameter and may be papular, vesicular or pustular, is considered positive. Lygranum antigen has also been used in complement fixation tests with 90 per cent accuracy. A biopsy may be taken which shows the granulomatous changes. There is usually an associated secondary anemia; the sedimentation rate is increased; and there is also a hyperglobulinemia with reversal of the A/G ratio.

The early stages other than the inguinal adenitis are rarely treated, because they are rarely recognized. The bubos may be incised. Fuadin and tartar emetic have been used. Sulfonamide derivatives are now used for the acute proctitis and ulcer stages. Frei antigen has also been used both subcutaneously and intravenously in gradually increasing

dosage. For the late rectal stricture x-ray, medicated enemas and dilatation of the rectum have been used with little effect. For advanced stricture colostomy, either alone or with resection of the rectum, may be necessary.

In obstetrical practice, we rarely see the acute phases of lymphogranuloma venereum since they are so ephemeral. The most common obstetrical complication is the rectal stricture. Even at that, lymphogranuloma venereum is an obstetrical rarity. This may be due to the fact that sterility is associated with the later stages of lymphogranuloma venereum. Some idea of its incidence may be gained by realizing that at the Chicago Lying-in Hospital, only one case has been seen in the past 10 years. In the Provident Hospital, Chicago, there have been 17 cases in the past 5 years. At the Sloane Hospital during the past 4 years, there have been 7 cases in 7,000 deliveries.

INCIDENCE OF LYMPHOGRANULOMA VENEREUM IN PREGNANCY

| | |
|--------------------|--------------------------------|
| Sloane Hospital | 1:1,000 |
| Provident Hospital | 17 cases in 5 years |
| Chicago Lying-in | 1 case in 10 years |
| New York Lying-in | 11 cases in 10 years (1:2,500) |

The largest series in the literature consists of 18 cases reported by Wilson and Hesseltine from Chicago. In this group, 2 therapeutic abortions were done because of marked perirectal fixation and previous colostomies. Of the remaining 16 patients, 13 delivered spontaneously, 1 was delivered by forceps, and 2 by cesarean section. Both cesarean sections were performed because of dystocia due to soft tissue masses. It is interesting to note that of the 14 patients who delivered spontaneously, 2 had colostomies.

LYMPHOGRANULOMA VENEREUM AT CHICAGO LYING-IN HOSPITAL

| |
|---|
| 18 Cases |
| 2 Therapeutic abortions (performed because of previous colostomy and perirectal fixation) |
| 16 Term deliveries |
| 1 Forceps |
| 13 Spontaneous |
| 2 Cesarean sections (because of dystocia caused by soft tissue masses) |

Of the 7 cases reported from Sloane Hospital, 1 was terminated at 4 months because of associated myomas as well as rectal stricture. Of the remaining 6 cases, 4 were delivered spontaneously and 2 by cesarean section. It is of passing interest to note that in one case a colostomy was performed simultaneously with the cesarean section. Their most interesting patient was a colored multipara who had had bleeding for 10 years from a rectal canal which was 0.4 cm. in diameter. The Frei test for 6 years had been positive as well. When she fell into labor, two weeks prior to term, the presentation was breech. As the cord prolapsed, it was replaced and a No. 3 Voorhees bag was inserted. Eight hours afterward, the patient was easily delivered of a stillborn infant, but 4

hours after delivery, she complained of abdominal pain and distention; 17 hours after delivery, an enema was given without return, and 21 hours after delivery she died. Autopsy revealed 1,500 c.c. of fluid in the peritoneal cavity, and a transverse rupture of the rectum above the site of the rectal stricture. A similar case is reported by Gaines and McDowell. An unregistered primigravida entered late in labor, at which time rectal examination revealed a tight stricture which extended as far as the finger can reach and marked thickening of the rectovaginal septum. After delivery by forceps was attempted unsuccessfully, a version and extraction were performed. The chin was impacted in the birth canal and was delivered only with great pressure. The patient died 5 hours following delivery, post mortem revealing a transverse tear in the rectum about 9 cm. above the anus. Unfortunately, there was no opportunity to do a Frei test.

Case Reports

In the past 11 years, there have been 11 patients with lymphogranuloma venereum in the New York Lying-in Hospital. The salient points in the histories of these patients will be briefly outlined:

1. E. N., a colored para 6, gravida 10, had a positive Frei test as the only evidence of her involvement with lymphogranuloma venereum. All her deliveries were uncomplicated.

2. D. M., a Porto Rican had a fistula-in-ano and a positive Frei test in 1933. There was no other evidence of the disease. Four years later in 1937, a full-term spontaneous delivery occurred.

3. R. W., a white multipara had an acute proctitis and a positive Frei test in February, 1938. In July, 1938, a spontaneous abortion occurred and in 1939, a full-term spontaneous delivery occurred. There was no stricture formation.

4. P. B., a colored para 0, gravida 3, had syphilis and a rectal stricture. She died in the sixth month of pregnancy of arsenical encephalitis.

5. C. M., a Porto Rican multipara had had 4 uneventful pregnancies. During her fifth pregnancy, she developed rectal bleeding, and pencil-like stools. An annular stricture was discovered 6 cm. above the sphincter; Frei test was positive and biopsy showed an acute granuloma. The delivery was without event.

6. E. W., a colored primipara had been known for the past 8 years to have a stricture about 5 cm. above the sphincter. Her Frei test was positive. Because of increasing constipation, a colostomy was contemplated, but was not performed because of the marked decrease in constipation which accompanied the pregnancy. An uneventful spontaneous delivery occurred.

7. A. W., a colored para 1, gravida 3 had two therapeutic abortions elsewhere because of a rectal stricture which began about 3 cm. above the sphincter. A full-term spontaneous delivery occurred after 6 hours of labor.

8. F. R., a colored multipara had previously had a colostomy performed because of rectal stricture. Her Frei test was questionable. In early labor, a vaginal examination revealed induration about the rectum

which is described as feeling like a "rubber pipe." A forceps delivery was performed with the accompaniment of a third degree tear.

9. E. P., a colored multipara had inguinal bubos 17 years previously, and had been constipated for 3 years. The Frei test was positive, and a rectal stricture was found 5 cm. above the sphincter. A vaginal examination in labor revealed no involvement of the posterior vaginal wall. A midforceps delivery was performed without difficulty.

10. R. M., a colored primigravida had noticed increasing constipation for 6 years and the Frei test had been positive for 2 years. At that time, a stricture was discovered 5 cm. above the sphincter. She was treated for associated lues. A vaginal examination during labor showed no fixation of the posterior vaginal wall. A low-forceps delivery was uneventfully performed.

11. H. M., this last case is reported in greater detail because it is the only case of lymphogranuloma venereum associated with rupture of the uterus that has been reported. The rupture, however, was not caused by the lymphogranuloma venereum as far as we can tell. This colored para 4, gravida 6, had been known to have a rectal stricture about 5 cm. above the sphincter, and a positive Frei test for 7 years. During this period, 4 spontaneous deliveries occurred. She was simultaneously treated for syphilis. The first stage occupied three hours. After 1 hour of second stage, the fetal heart slowed. The patient who had previously been noisy, became quiet. The nurse who was holding the fundus stated that it changed in shape. Since the vertex was on the perineum in R.O.A. position, preparations were made for a forceps delivery. The right blade of the forceps was readily inserted. As the operator's left hand was inserted into the vagina preparatory to the application of the left blade, the head rose out of the pelvis and the patient's blood pressure abruptly dropped to 65/40. Acting on the diagnosis of rupture of the uterus, a laparotomy was immediately performed. On opening the peritoneum, a deadborn infant and the placenta were found lying free in the peritoneal cavity. On the anterior half of the lower uterine segment just below the level of the internal os, was a semicircular site of rupture which closely resembled the incision for subtotal hysterectomy. A subtotal hysterectomy was performed. The pathologic report stated that there was no involvement of the pericervical tissue by lymphogranuloma venereum. The patient had an uncomplicated postoperative course.

NEW YORK HOSPITAL—EXPERIENCE

11 Patients

3 Without stricture

- 1 Positive Frei test alone
- 1 Fistula-in-ano
- 1 Acute proctitis

8 With stricture

- 1 Died of arsenical encephalitis occurring in the sixth month of pregnancy
- 3 Delivered spontaneously
- 3 Delivered by forceps
- 1 Delivered by cesarean section (rupture of uterus)

It is of note that one of the patients who delivered vaginally, had a colostomy of 10 years' standing.

The last point of interest is whether lymphogranuloma venereum is transmitted to the fetus. Most observers believe that if it is, it is not

by intrauterine spread, but rather during and after birth. Dick has reported many positive Frei tests in early life. Wilson performed Frei tests on 13 babies; 12 of these were negative; the thirteenth which was positive on the infant's third and tenth days was negative at three months. It has been adequately proved that lymphogranuloma venereum per se does not increase the stillborn rate.

Summary and Conclusions

In reviewing these histories, certain factors stand out. The patients are usually colored. They are almost invariably syphilitic as well, so that when patients have a rare venereal disease one can almost infer that they will have a more common venereal disease. These patients are frequently anemic. In deciding upon the type of delivery, a vaginal examination before the onset of labor or in early labor will give the most information. If there is marked perirectal fibrosis, or soft tissue masses, or fixation of the posterior vaginal wall, vaginal delivery will be fraught with difficulty and danger. It is interesting to note that in both the cases of rupture of the rectum, breech extraction was performed. Hence, when the presentation is breech in a woman with a stricture of the rectum, external cephalic version should be attempted.

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CALCIFICATION IN CEPHALHEMATOMATA OF THE NEWBORN INFANT

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CEPHALHEMATOMATA of the newborn infant are localized collections of blood beneath the periosteum of one of the bones of the cranial vault. They may be single or multiple. The entire periosteum covering that particular cranial bone is elevated. Cephalhematomata may appear after a normal delivery, but they are certainly more frequent after long hard labors, particularly if there has been operative interference.

The lesions themselves are not particularly dangerous, but since they are more common after difficult labors, babies presenting them bear most careful watching. The swelling appears the first or second day after delivery, and usually absorbs rapidly after the first week of life. Most of them are completely absorbed by the third week. Since they usually run this innocuous course, the common plan of treatment is one of utmost conservatism. The mothers who are naturally alarmed by this unsightly bump on their babies' heads are bluntly told, "Forget about it. It will go away."

Unfortunately, all of them do not go away. A very appreciable number calcify, forming a more or less permanent deforming lump on the child's head. While this lump is of importance only from the cosmetic standpoint, it causes the parents great concern. Since its presence can be easily prevented, we believe that more attention should be paid to the treatment of these lesions.

The pathogenesis of this calcification is of interest. As has been noted, the collection of blood is beneath the periosteum of one of the flat bones of the skull. The periosteum is adherent to the bone at its margin, and can be elevated over its entire surface. The hematoma, therefore, is sharply delineated by the margins of the particular bone which it happens to overlay. In one of the lesions which does not absorb rapidly, subperiosteal osteogenesis begins at the attached margin of periosteum all around the circumference of the bone. If absorption of the clot is completed at this time, the newly formed bone can be felt as a slight ridge or elevation around the edge of the skull plate. This gives a false sensation that the central portion of this particular bone is depressed and can be mistaken for a depressed skull fracture.

If, however, absorption of the clot does not proceed rapidly, the newly formed bone at the edge grows subperiosteally up over the dome of the bulge until at one stage only a small area at the apex of the lesion lacks a bony covering. Shortly, this is also filled in, and the hematoma is

completely roofed over with a thin pliable layer of bone. This bony covering rapidly becomes thicker and more solid until in a few weeks it clinically seems as firm as the remainder of the skull. We have serial radiographs depicting the various stages of this development.

There is now a hard bony protuberance which persists for an indefinite-length of time. As the child grows, the protrusion seems to tend to flatten and merge into the general contour of the skull, but it is an extremely slow process.



Fig. 1.—Cephalhematoma completely roofed with bone, in infant five weeks old.

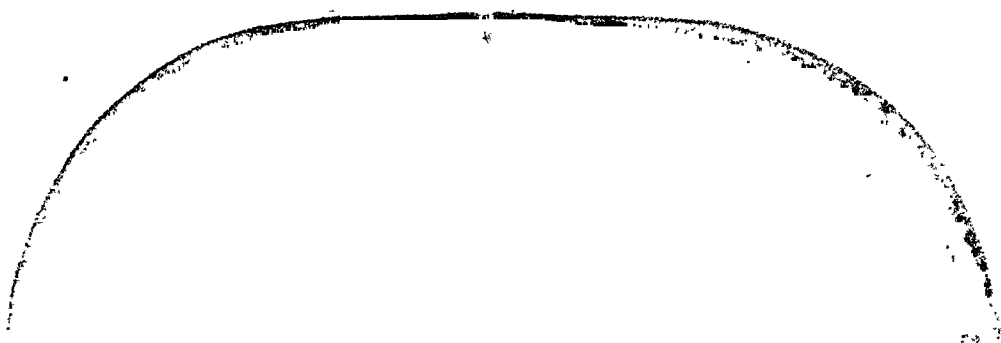


Fig. 2.—Bilateral calcified lesions persisting in child two and one-half years old.

Three radiographs illustrating the condition are presented. Fig. 1 shows a lesion completely calcified in a baby five weeks of age. Fig. 2 shows bilateral calcified lesions on the skull of a child two and one-half years of age. These had given the child's head a peculiar heart-shaped outline which, combined with a lack of hair had caused the parents great mental perturbation. These lesions are now flattening out and will probably disappear in time. Fig. 3 shows a well-marked lesion on the head of a boy ten years of age.

Dr. S. J. Webster, of Cleveland, followed one lesion which persisted for more than twenty years. Therefore, while the tendency may be toward spontaneous cure it can certainly be slow.

We have elaborated on the natural life cycle of these lesions in order to make our point concerning their treatment. As we have mentioned, absolute conservatism is usually advised. Christopher¹ mentions that Cushing has tried incising cephalhematomata and evacuating the clots. He is, however, hesitant to do so because of danger of infection. Very little has ever been mentioned in English literature concerning calcification of a cephalhematoma. No reference to the possibility was found since 1935. Two articles stressing the possibility have appeared in German journals during the same period. Kastendieck² presented several cases in which ossification occurred. He felt that the cosmetic result was distressing, and mentioned that incision and evacuation of the clot might be tried as prophylaxis. However, he also felt that the danger of infection probably made such a procedure unjustifiable. Ottow³ presented several cases in which calcification occurred, but made no mention of treatment either prophylactic or active.

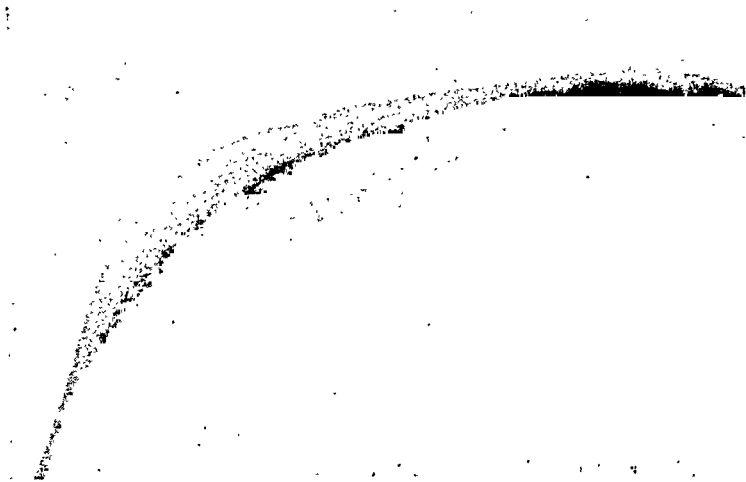


Fig. 3.—Large calcified cephalhematoma on skull of child ten years old.

From our experience we cannot agree with this absolute conservatism. We feel that the lesion should be closely watched. At the end of two weeks, most of them are absorbing rapidly. These should, of course, be left alone. In those which are not absorbing rapidly by this time, it will be found that the contents have liquified and may be easily aspirated. If a fairly large bore needle is introduced beneath the elevated periosteum, from ten to forty cubic centimeters of thick bloody liquid can be withdrawn. The cyst then largely collapses; the small amount of remaining contents rapidly absorbs and permanent deformity is prevented.

By use of standard aseptic technique, we can see no more reason to fear infection in these cases than in any other minor surgical procedure. In the past five years we have routinely aspirated those which did not absorb rapidly, and have had no trouble at all. One of the first ones which we aspirated had been allowed to progress until a thin layer of

bone entirely covered the dome of the hematomata. We introduced a stout needle through this light layer of bone and aspirated forty cubic centimeters of bloody fluid. We then mashed the fragile osseous dome down upon the underlying bone of the skull. The pieces of it could be palpated lying under the skin and periosteum, feeling like small bits of crushed egg shell. This rapidly absorbed, giving a perfect cosmetic result. On the other hand, the persistence of an unsightly bony protuberance on the baby's head is most distressing. It undoubtedly causes no untoward functional results, but is certainly a negative advertisement for the obstetrician's skill, vitiating what may otherwise have been an able or even brilliant delivery.

Summary

Attention is called to the fact that ossification not infrequently occurs in cephalhematomata of the newborn infant. Aspiration of lesions not absorbing rapidly is advocated to prevent unsightly deformity of the skull.

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INFLUENCE OF EPINEPHRINE UPON THE HUMAN GRAVID UTERUS*

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RUCKER¹ in 1925, called attention to the fact that studies published concerning the action of epinephrine showed opposite effects in different animals and even in the same species of animals with various conditions of the uterus. In his studies on intrauterine pressures of 20 pregnant human beings, he observed that epinephrine decreased uterine activity in 80 per cent of the patients. The results of Bourne² and of those from this laboratory³ indicate that in human beings, epinephrine causes an initial brief period of increased activity followed by a short period of reduced uterine activity. Recently, Brown and Wilder⁴⁻⁶ quote these latter studies to disprove Rucker's statement that epinephrine relaxes the uterus. It is a common pharmacologic observation that epinephrine in proper dosage can produce either excitatory and/or inhibitory effects upon a number of structures innervated by the sympathetic nervous system. Both actions may be present and may tend to counterbalance each other. The present studies were undertaken to determine whether epinephrine has both stimulatory and inhibitory actions upon the human pregnant uterus.

Methods

As previously described^{3, 7} a balloon tied to a catheter was inserted into the uterus of patients pregnant 9 months. The balloon was then partially filled with 30 c.c. of 0.6 per cent sterile sulfanilamide solution. The balloon and catheter, by acting as a foreign body, soon induced uterine contractions. After contractions were well established, epinephrine was injected intravenously in doses ranging from 0.01 mg to 0.1 mg. The rate of injection was varied. Rapid injection requiring 3 seconds was used to simulate the usual intravenous administration. Dilution of 0.01 and 0.02 mg. of epinephrine in 20 c.c. saline allowed slow injections requiring six to ten minutes. This simulated the gradual absorption resulting from intramuscular or subcutaneous administrations. The injections of epinephrine were separated by periods of 10 to 15 minutes to permit recovery from previous administrations.

Results

The effects of epinephrine upon the intact gravid human uterus were found to differ with the drug concentration present at the site of action.

*Aid from a grant from Eli Lilly and Company is gratefully acknowledged.

Rapid intravenous injection of 0.1 mg. (see injection 1) caused immediate strong uterine contractions which followed each other so closely that the uterine pressure remained elevated between contractions. The increased frequency is evidence of heightened excitability, the faster rise of pressure during onset of contraction and the shorter duration of the contraction suggest that the epinephrine induced contraction may not be the normal peristaltic-like type of contraction. Two and one-half minutes after the injection the uterine pressure was low, and there was only slight evidence of uterine activity for three and one-half minutes. These results are in agreement with previously published observations of the effect of intravenous administrations.²⁻⁴ Bourne and this laboratory have interpreted such records to indicate that epinephrine causes a delayed inhibition of uterine activity after the transient initial increased activity. Even though the pressures are low, Brown and Wilder interpret this delayed effect of epinephrine as evidence of sustained muscular activity.

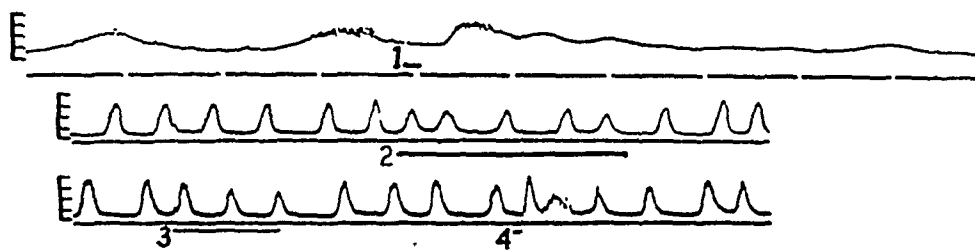


Fig. 1.—Intrauterine pressures from gravid patients recorded by direct Method. Pressure scales are shown in units of 25 mm. Hg; base lines are interrupted at one minute intervals. Solid lines above or below the time line indicate duration of injection.

1. Epinephrine 0.1 mg. in 1:1,000 dilution was injected rapidly. Note that premature contractions resulted, and that amplitude and frequency were increased. This interval of hyperactivity was followed by a period of relative quiescence.
2. Epinephrine 0.01 mg. in 1:2,000,000 dilution injected slowly. Note that amplitude of uterine contractions was decreased during time of injection, but there was no significant change in frequency or tone.
3. Epinephrine 0.02 mg. in 1:1,000,000 dilution injected approximately twice as fast as in No. 2. Amplitude of contractions again reduced, but there was no significant decrease in tone or frequency. Secured from same patient as No. 2.
4. Epinephrine 0.05 mg. in 1:10,000 dilution injected rapidly. Note marked increase in amplitude of epinephrine induced contraction following injection, followed by three contractions of decreased amplitude. Secured from same patient as No. 2 and No. 3.

It seems reasonable that the action upon the uterus might resemble that upon other structures such as the blood vessels in which inhibitory effects of epinephrine are present, and outlast the excitant effects. Since small doses can elicit this inhibitory action on blood vessels, it was considered advisable to determine their effect upon the human gravid uterus. The amplitude of the uterine contractions was decreased when small doses of 0.01 and 0.02 mg. epinephrine, respectively, in a 1:2,000,000 and 1:1,000,000 dilutions were administered slowly over a period of six to ten minutes (see injection 2 and 3). These slow injections simulate the decreased rate of absorption which occurs with hypodermic administrations. These inhibitory effects are in entire agreement with the previously published observations of Rucker,¹ who usually administered the drug by the hypodermic avenue. Divergent results from different laboratories may sometimes be explained by the fact that the drug was administered by different routes.

Summary and Conclusions

The rate and avenue of administering epinephrine influences its effect upon the human gravid uterus. Administered subcutaneously, intramuscularly or very slowly intravenously, small doses reduce the amplitude of uterine contractions. Administered in larger doses, heightened uterine activity precedes the inhibition, and both effects are pronounced. These observations concern only the normal gravid uterus, but they do suggest that epinephrine may reduce Bandl's ring and retraction rings if they occur.

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COEXISTENT ECTOPIC AND UTERINE PREGNANCY

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SIMULTANEOUS intrauterine and extrauterine pregnancy is one of the less common obstetrical complications. It is to be differentiated from *compound* pregnancy which is a term used to designate pregnancy intrautero superimposed on an older ectopic pregnancy which has resulted in lithopedion formation.¹ This differentiation may account for the rather considerable variation in the total number of cases reviewed by various authors.² It can be said, however, that over 300 cases of simultaneous intrauterine and extrauterine pregnancy have been reported.³

Most of these cases appear to be twin pregnancies, although some apparently are gestations superimposed on those previously existing.⁴ The condition appears to be more common during the latter part of the childbearing period, in multiparas, and in women who have a family history of multiple pregnancy. The extrauterine pregnancy may be ovarian, tubal, or abdominal.

The importance of the condition lies in the difficulty of making a correct diagnosis and in its high mortality. In one series of 170 cases, the correct preoperative diagnosis was made in only 7 cases, and in another series of 32 cases, the preoperative diagnosis was correct in only 3 instances.³ Most commonly, the picture in early cases seems to be that of an ectopic pregnancy. Enlargement of the uterus is then considered to be only that usually seen associated with an ectopic pregnancy, and the intrauterine gestation is overlooked unless there be signs of an impending abortion.³ Indeed, it may happen that the uterine abortion precedes the rupture of the tubal pregnancy. More than forty cases of this kind have been reported.⁵

The seriousness of the condition is shown by the fact that the mortality rate for the whole series of 217 cases reviewed by Gemmell and Murray⁵ was 20.7 per cent. After excluding the cases in which the diagnosis was made only at autopsy, the rate was 14.4 per cent.

It seems to be generally agreed that the only treatment is surgical. It is advised that if the condition is discovered in the early months of pregnancy and both fetuses are living, the ectopic pregnancy should be removed. If both fetuses are living in the late months, the treatment is expectant, with laparotomy at term. If the ectopic fetus appears to be dead, removal is commonly advised; otherwise, some of these patients pass the fetus piecemeal through fistulas.⁵

Case Report

M. M., a 32-year-old housewife, mother of four children, was first seen August 27, 1943, complaining of occasional nausea, and of ab-

normal flow. Her last menstrual period had begun July 15. August 6, three weeks before being seen, she had begun to have occasional episodes of slight nausea. A week later, she began to pass a few drops of dark red blood each day. Three days later she had a stem pessary, which had been inserted by an osteopath for contraceptive purposes, removed. Her symptoms continued.

On physical examination at this time, August 27, she was afebrile, and was slightly tender over all of her lower abdomen. There was a sensation of a small suprapubic mass. On pelvic examination, the uterus seemed enlarged to the size of a three months' pregnancy; the cervix seemed slightly soft. The breasts were negative. The impression was that the patient was probably pregnant intrauterine, and was threatening to abort, or that she had intramural fibroids. Urine was obtained for an Aschheim-Zondek test, and the patient was sent home to bed.

Three days later, the patient was seen at home complaining that on two consecutive mornings she had had rather severe lower abdominal cramps, similar to labor pains, and of sufficient severity so that she had wept with them. At the time of the cramps on the first day, she had had enough bright red flow to require one or two pads, but on the second morning, the flow had become dark brown in color, and was only slight in degree. Hospitalization was advised, and was carried out the same day.

The patient's past history was not of interest except for her menstrual and marital histories. Her catamenia had begun at thirteen, had always been regular in a 28-day cycle lasting 4 to 5 days without pain. She had married at 17 years of age, and had not become pregnant for six years, in spite of using no contraceptive precautions. She had then had four uncomplicated pregnancies preceding her present illness, her youngest child being three years of age.

One maternal great grandfather was a twin, and his wife was also a twin. The patient's brother was the father of twin sons. There was no twinning among the husband's relatives. The systemic review was noncontributory.

The positive physical findings of interest were limited to the abdomen and pelvis. The abdomen was obese. The upper quadrants were negative to palpation. The lower midabdomen was slightly tender, and there was a sensation of suprapubic resistance. There was very slight tenderness, and very slight rebound tenderness in both lower quadrants. The perineum was relaxed. Bluish discoloration of the vulva was not noted. The vaginal wall was not unusual. The cervix seemed slightly soft. Pain was induced on motion of the cervix. The uterus was enlarged to approximately the size of a three months' pregnancy. No masses were palpable in the adnexa. Both adnexal areas were very slightly tender. There was no bulging or tenderness in the cul-de-sac.

Examination of the urine showed a pale amber, cloudy specimen, of acid reaction and with a specific gravity of 1.018. Albumin 0, sugar 0, acetone four plus. The sediment showed an occasional white blood cell, a few red blood cells, and a moderate number of epithelial cells. The hemoglobin was 88 per cent (Sahli); R.B.C. 4,380,000; W.B.C. 6,950. There were 74 per cent polymorphonuclear cells, 23 per cent lymphocytes, 2 per cent stab cells, and 1 per cent basophils. The Kahn test was negative. A preliminary diagnosis of intrauterine pregnancy

with threatened abortion was made, with the possibility of an extra-uterine pregnancy indicated as a second choice.

The patient's hospital course was uneventful and afreble. She continued to have a small amount of dark brown, foul-smelling discharge, but did not have any cramps while in the hospital. She was given 1 mg. of progesterone intramuscularly daily. The Aschheim-Zondek test taken before admission was reported positive. On September 4, 1943, five days after admission, pelvic examination showed no tenderness or masses in the vaults, nor any tenderness in the cul-de-sac. The patient was discharged with a final diagnosis of threatened abortion.

At home she stayed in bed, and progesterone was given every second day. After riding home in a car, her bleeding increased slightly for one day, but this subsided so that she simply spotted a small amount of brown discharge daily. There was no more pain. Gradually she got up and about, and five days later came into the office complaining of being weak and chilly. She had no fever. The hemoglobin was 88 per cent (Haden-Hausser). The progesterone was stopped, the patient was allowed restricted activity and was told to return in a week.

Five weeks later, she returned saying that she felt somewhat weak and had little appetite. She had had no more pain. She continued, however, to have a small amount of brown discharge. At this time, the fundus was felt 4 cm. below the umbilicus. The blood pressure was 110/70; weight 173 pounds. The urine was normal. The pelvis was not examined.

Three weeks later, November 8, 1943, sixteen weeks after onset of her last normal menstrual period, the patient was seen at 11 A.M. at home, complaining of recurrence that morning of lower abdominal pain. The pain was steady, and radiated down the anterior aspect of the right leg. The fundus was just below the umbilicus, and was slightly tender. There was a slight tenderness in the left lower quadrant. Since it was thought the patient might be miscarrying, a rectal rather than a pelvic examination was made. The cervix was closed. No conclusions regarding the vaults could be drawn from rectal examination. The pain was not severe. She was given medication for pain, and was told she would be seen again in the evening unless she reported signs of impending termination of her pregnancy.

Six hours later, the family called saying that the patient had been vomiting ever since shortly after the morning visit, and that the pain had become more severe. At first glance, it was obvious she had been bleeding internally, although her blood pressure was 110/50, and her pulse 96. She was pale and sweating. She was given morphine sulfate gr. $\frac{1}{6}$ subcutaneously, and an attempt was made to secure an ambulance immediately. When she was placed in the ambulance, an intravenous infusion of 5 per cent glucose in saline solution was begun, but it would not run due to our inability to raise the flask high enough. Because of delays in getting an ambulance and distance, it was 4½ hours before the patient could be admitted to the hospital 27 miles away.

On admission, temperature was 98.8, respiration 20, pulse 100, and blood pressure 110/40. The patient was pale, sweating, complaining of abdominal pain, fullness in the abdomen, and shortness of breath. The mucous membranes were extremely pale; the tongue was dry. The lungs were clear. The heart was negative. The abdomen appeared distended, and there was very acute tenderness and spasm throughout.

The fundus could be felt just below the umbilicus. Since it was apparent that surgery was necessary, pelvic examination was omitted.

The hemoglobin was 61 per cent (Sahli); R.B.C. 3,500,000, W.B.C. 12,550 with 75 per cent polymorphonuclear cells, 16 per cent lymphocytes; 4 per cent stab cells; and 2 per cent eosinophiles. The urine (catheterized) was clear, yellow, specific gravity 1.018. Albumin, faint trace, sugar 0, acetone ++, 4 to 6 W.B.C. per high power field, and an occasional hyaline cast.

Preliminary diagnoses were intrauterine pregnancy; intra-abdominal hemorrhage of unknown cause; possible ovarian cyst twisted on a pedicle; possible pedunculated uterine fibroid twisted on a pedicle.

Operation: (D.E.E.) Under nitrous oxide, oxygen, and ether anesthesia the abdomen was opened through a suprapubic midline incision. Upon opening the peritoneal cavity, a large amount of blood was encountered. This was removed by suction and collected in a sterile flask, which contained citrate. As much liquid blood and blood clots as possible were removed. It was estimated that this amounted to about 2,000 cubic centimeters. The uterus was enlarged, soft and consistent with a 4 to 5 months' pregnancy. The right tube and ovary were normal. The left tube and ovary were the site of ectopic pregnancy, which had ruptured. There was a large rent, about 5 cm. long, in the tube, from which there was free bleeding. Clamps were applied, and the tube and ovary on the left were removed. Double transfixing catgut ligatures were applied and the clamps removed. The abdomen was closed in layers without draining.

The specimen was examined and found to contain the head of a macerated fetus, about 2.5 cm. in diameter. The remainder of the body was not found.

Subsequent Course.—During the operation the patient was given one unit of plasma and 500 c.c. of citrated blood. Following the operation, her condition was relatively good, her blood pressure having been maintained, and her pulse not having become elevated. After she had been returned to her room, 1,000 c.c. of the blood which had been removed from her abdominal cavity was given.

Her postoperative course was uneventful. She had not felt fetal motion. On the tenth postoperative day, a film of the abdomen was taken but there was no evidence of fetal skeleton. This brought up the possibility of the enlargement of the uterus being due to a hydatidiform mole, or to fibroids. The patient was discharged from the hospital fifteen days after operation. An Aschheim-Zondek test at this time was positive. There had been no vaginal bleeding.

Six days later, the patient felt fetal motion strongly, although the fetal heart was not as yet audible.

The remainder of the patient's course was uneventful. Throughout her pregnancy, the size of the fundus seemed to be greater than was reasonably to be expected. It was suspected that the intrauterine pregnancy might be a twin one, but two heads were not palpable, nor were two hearts audible, and on April 3, 1944, a plain film of the abdomen showed only one fetus. The calculated due date was April 22, and on April 26, at 11 P.M., the patient began to have mild uterine contractions. Six hours later, after a relatively easy labor, a 10-pound male infant was delivered from left occiput anterior position. There seemed to be a definite increase in the amount of amniotic fluid, which, together with the large size of the infant, probably accounted for the large size of the uterus.

Comment

In the series of cases reviewed from the literature by Gemmell and Murray,⁵ there were 93 in whom the condition was discovered in the first half of the pregnancy, before abortion of the uterine ovum. Of these, 36 aborted postoperatively, and 32 carried the intrauterine pregnancy to term. After attempting to analyze their data, they conclude that there are no definite criteria on which to base the prognosis of the intrauterine ovum postoperatively, although they have the impression that those patients having a large amount of intraperitoneal blood are more apt to miscarry. Details regarding the corpus luteum in the various case reports are scant, but it is known that not all of the patients in whom it was removed miscarried, and, on the contrary, some in whom it was left did miscarry. No notice of the corpus luteum was made in our case, nor was it mentioned in the pathologic report.

From the size of the macerated fetal skull removed at operation, it would appear that this was an instance of twin pregnancy, and that the circumstances which led to the patient's first hospitalization were concerned either with a threatened abortion of the uterine ovum, or with a beginning rupture of the ectopic pregnancy. We made the mistake opposite to that usually made; i.e., we considered the situation to be an intrauterine pregnancy alone, whereas it appears to be more common to consider that the pregnancy is ectopic alone. The unusual size of the uterus with relation to the menstrual history led us in this direction.

Summary

Coincidental intrauterine and extrauterine pregnancy is a relatively uncommon complication of pregnancy, dangerous both for the mother and for the intrauterine ovum. A case is reported in which the intrauterine ovum was carried to term.

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SUPRACERVICAL PREGNANCY FOLLOWING SUPRA-VAGINAL HYSTERECTOMY

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SUPRACERVICAL pregnancy following hysterectomy is a very rare occurrence. There are reports of 6 cases of pregnancies following hysterectomies, of which 4 were tubal, 1 extrauterine and 1 in the cul-de-sac posterior to the bladder. Two of these patients died of hemorrhage; two had the pregnancies removed by operation; one had a 7 months' child delivered by laparotomy, and one had a 6 months' child delivered from the cervix. Because of its unusual location, the following case was thought worth while reporting:

Mrs. P., white, aged 34, was seen for the first time by one of us (F. E. S.) on October 5, 1933. She was pregnant. The expected date of delivery was February 27, 1934. Physical examination and Wassermann test were negative. Prenatal course uneventful except for nausea and some vomiting in first 3 months. Delivered (F. E. S.) February 28, 1934, midforceps, because of midpelvic arrest, and median episiotomy. Patient was seen at intervals until 1937, when she was again pregnant. Prenatal course uneventful except for nausea and some vomiting in first three months. Delivered (F. E. S.) spontaneously July 24, 1938. In August, 1939, she complained of bearing down pains in pelvis, short menstrual cycles. On examination "uterus larger and firmer than would be expected. No definite tumor outlined." Irregular bleeding increased and in December, 1939, a curettage was done (F. E. S.). Pathological report: "Glandular hyperplasia with marked hyperplasia of stroma." Following this, the periods were regular and normal.

In August, 1941, she complained of backache. On examination, a fibroid was easily distinguished in fundus. Uterus was slightly enlarged. Pessary was introduced. Backache was relieved.

In January, 1942, patient was told that if she wanted another baby to plan it soon. Patient said she and her husband had decided against another pregnancy.

In April, 1943, uterine fibroid definitely larger. Surgical consultation (M. S.-B.). Hysterectomy advised.

Patient was admitted to Booth Hospital June 5, 1943, and a supra-cervical hysterectomy was done (M. S.-B.) on June 6. The uterus was amputated at the uterocervical junction without removing the tubes and ovaries. The cervical stump was closed with 4 interrupted chromic sutures. The ligated tubes and round ligaments were sutured to the posterior lip of the cervical stump and the vesicle fold was brought over to cover the area. The patient made an uneventful recovery. Following this and until March, 1944, patient was well and had no complaints. She had fairly regular, scanty monthly bleeding. On March 20, 1944, patient was seen by both of us. She had missed one period. She was nauseated, having a few hot flashes and occasional lower abdominal

pains. On examination, cervix seemed well suspended, adnexa negative, no pathologic condition found. Endocrine therapy helped patient's symptoms.

Patient reported a flare-up of nausea and abdominal pain April 12, 1944. Examination at this time showed a softer cervix and immediately above it a small, soft mass. The nausea increased and the picture duplicated that of her two previous pregnancies. On examination, the mass was definitely larger and a diagnosis was made of a supravaginal pregnancy of about 6 weeks. Patient entered the hospital on April 28.

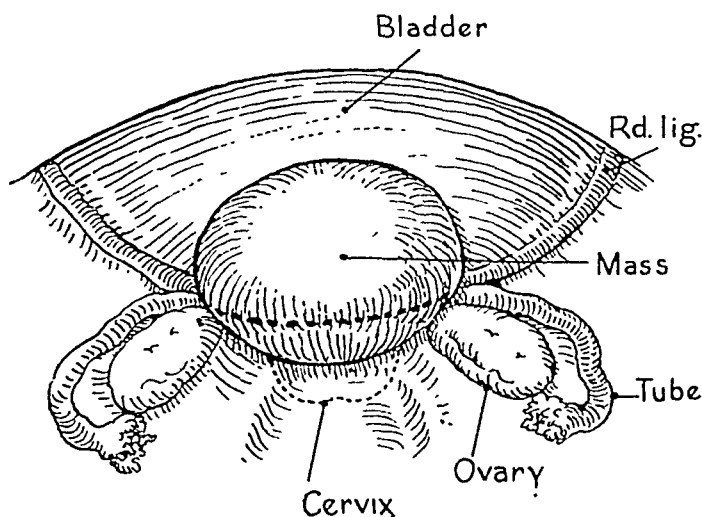


Fig. 1.

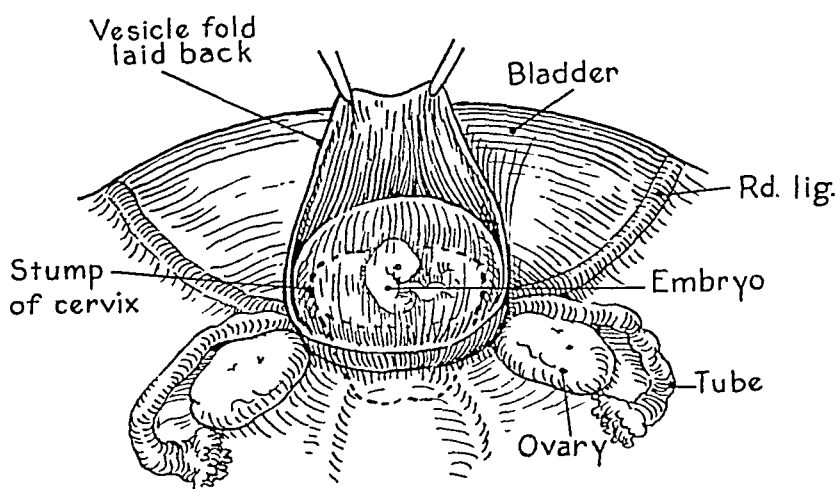


Fig. 2.

On April 29, 1944, an exploratory laparotomy was done. The abdomen was opened through the old midline scar which had become hypertrophied and pigmented. The pelvis was inspected. There were a few adhesions which were freed and the vesicle fold with the round ligaments and tubes was found to have been stretched upward by a mass situated apparently on the cervical stump. (Fig. 1.) The vesicle fold was dissected free and laid back. Beneath the fold, there appeared tissue which resembled placenta, and from this by blunt dissection, a sac of fluid containing a 6½ weeks' embryo was shelled out intact. (Fig. 2.) As much placental tissue as possible was removed, and the stump

of the cervix closed with chromic sutures. The tubes were both resected and the round ligaments resutured to the posterior lip of the cervix. The vesicle fold was brought down over the stump and ligaments. The wound was closed in layers. The patient made an uneventful recovery, and was discharged on the fourteenth day after operation.

Examination on June 2, showed the wound was well healed, pelvis negative and her general condition excellent.

Follow-Up Note.—Patient seen during the month of October, and found to be in good condition.

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ORTHOSTATIC ALBUMINURIA DEVELOPING LATE IN PREGNANCY*

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THIS case is reported because first, it presented a trying if not serious diagnostic problem and, second, in a rather extensive and careful perusal of the literature and standard textbooks on obstetrics, no mention is made of the condition other than in the few instances cited here. It is the author's opinion that an occasional case diagnosed as mild pre-eclampsia or "low reserve kidney" of Stander and Peckham, may be in fact nothing more than orthostatic albuminuria developing late in pregnancy. Indeed, it is well known that in the later months of pregnancy, when the gravida assumes the erect posture, there is a tendency toward exaggerated lordosis, and lordosis is believed to be the principal cause of orthostatic albuminuria.

The case reported below might well have been put at strict bed rest or even hospitalized with a resultant clearing of the albumin from the urine. The obstetrician would then have felt that the bed rest plus the usual dietary restriction effected the "cure."

F. Cook and V. E. Lloyd¹ report a case of albuminuria occurring late in pregnancy. Their patient, when put to bed, had no albumin in her urine but, the moment she was allowed up, the albumin recurred. No diagnosis was made, nor were any conclusions drawn from this case. G. W. Theobald,² in a very comprehensive article, suggests the possibility of a mechanical albuminuria of pregnancy. He further states: "Albuminuria, per se, bears no relationship to the toxemias of pregnancy." However, no specific cases are cited. P. Balard³ reports the case of a woman who had orthostatic albuminuria from adolescence until the time she became pregnant. During her pregnancy the albuminuria disappeared.

Case Report

S. A., white, 26 years of age, a private patient, was first seen at my office on April 22, 1941. At that time, she was pregnant for the first time, and her prenatal course was uneventful. Bi-weekly blood pressure determinations and urine examinations were normal. She did have a rather pronounced anemia which was treated with iron per os and liver injections. She was delivered at term of a 5-pound 5-ounce normal female infant, and the postpartum period was without incident. The patient was next seen on August 6, 1943, at which time she was again pregnant. Her last menstrual period was June 13, 1943, and the computed date of confinement was March 20, 1944. The Wassermann test was negative, and the hemoglobin 80 per cent (Sahli). Nevertheless, a ferrous iron was immediately prescribed, but, notwithstanding this, within 2½ months, the patient's hemoglobin had again fallen to 60 per cent (the same as her last pregnancy). The patient's prenatal course was again otherwise uneventful, and she stated that she felt better during this pregnancy than she had in years.

*Read at a meeting of the Section on Obstetrics and Gynecology of the New York Academy of Medicine, May 23, 1944.

At the onset of her pregnancy, the patient weighed 140 pounds; at the beginning of the ninth calendar month, she weighed 160 pounds. She was seen at the office on February 15, 1944 and a marked trace of albumin was found in the urine; the blood pressure was 115/70. It was felt that this albumin might have been the result of vaginal contamination. On questioning, the patient stated that she had had no headaches, though she had suffered with them frequently prior to the onset of this pregnancy. There was no sign of edema of the face or extremities. A specimen of urine sent to the office three days later contained two-plus albumin, and microscopic examination of the urinary sediment showed an occasional hyaline and finely granular cast, but no red blood cells. This microscopic picture remained unchanged until delivery. Her blood pressure was 120/65, weight 161 pounds, and a specimen taken at that time showed four-plus albumin. There were no subjective complaints nor was there any edema.

She was put on a rest regime and told to eat nothing but small quantities of fruits and vegetables, cooked without salt, and to drink 4 to 6 glasses of milk a day. Four days later, the urine boiled almost solid with albumin, but the patient's blood pressure and weight were unchanged. For the next two days there was no change.

By this time the patient was somewhat disgusted. She stated that she had felt fine until the albumin was found in her urine, but the diet plus the rest regime were "running her down." However, the importance of maintaining this routine was explained and the patient continued to cooperate. She returned to the office three additional times at three-day intervals; each time the urine was loaded with albumin, the blood pressure was 115/60 and her weight remained the same. Subjective symptoms of toxemia and edema were absent. She was then told to do the following:

One hour after retiring, empty her bladder in a bedpan and discard that urine. The following morning she was again to empty her bladder in a bedpan, without getting to her feet, and bring that specimen to the office. When she arrived at the office, she was again asked to void. The two specimens were examined and the one voided early in the morning was found to be albumin-free, whereas the one taken at the office boiled almost solid. This same procedure was repeated on three successive days with the same results.

It was the author's opinion that this was a case of orthostatic albuminuria developing late in pregnancy. Ophthalmologic eye ground studies were reported as perfectly normal. Various laboratory procedures were then carried out. The results were as follows:

Blood Count—3/14/44

Hemoglobin—73%
R.B.C.—3.75 million
W.B.C.—16,800
Platelets—190,000
Myelocytes-Neut.—2%
Polys, nonsegmented—29%
Polys, segmented—54%
Lymphocytes—10%
Monocytes—5%

Blood Chemistry

Glucose—89 mg. %
Van Slyke Index—41 (Standard clearance)
Urea nitrogen—11.7 mg. %
Uric acid—1.9 mg. %
Albumin-Globulin ratio—2.7

Fractional Phenolsulfonphthalein Test for Kidney Function

| | | | |
|-------------------------|-----|-------------------------|----|
| After first 15 minutes | 18% | After fourth 15 minutes | 8% |
| After second 15 minutes | 22% | After fifth 15 minutes | 6% |
| After third 15 minutes | 19% | After sixth 15 minutes | 4% |

On March 17, the head was found to be fairly well engaged and the patient was told to take two ounces of castor oil. She went into labor at 6 o'clock that evening, and was delivered of a normal female infant, weighing 5 pounds 9 ounces, five hours later. The postpartum course was entirely normal, and urine examination (catheterized), on two separate occasions, revealed neither albumin nor casts. The patient was discharged from the hospital on the thirteenth postpartum day. On four subsequent occasions, covering a period of three weeks, her urine was examined and found to contain neither albumin nor casts.

Summary

A case of orthostatic albuminuria occurring late in pregnancy is detailed. This diagnosis is probably indisputable, nevertheless, in fairness we may point out the following: The blood count showed a leucocytosis and a shift to the left in the differential; however, this is surely not the blood picture of a toxemia; the Van Slyke index standard clearance is at the lower limits of normal; the fractional phenolsulfonphthalein test shows a delayed excretion, but we may explain this by the fact that the patient was at term, and there is a known hydronephrosis and hydroureter late in pregnancy. Finally, the absence of subjective symptoms, the occurrence of albumin in the urine only on assuming the erect posture, the normal weight gain, the absence of edema of the face or extremities, the repeatedly normal blood pressure readings, the absence of eye ground changes, plus the essentially normal blood findings, all confirm the diagnosis.

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20 EAST 76TH STREET

AN UNUSUAL CASE OF ALLERGIC (ANGIONEUROTIC) EDEMA AND OLIGURIA ASSOCIATED WITH PREGNANCY

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ANGIONEUROTIC edema is not uncommon; when extremely marked and associated with pregnancy, it is infrequent and, fortunately, relatively rare. This report is recorded because of the unusual and bizarre complications that may arise during the pregnant state.

Mrs. B. C. presented herself at the office on 10/21/43 some 16 weeks pregnant. From the obstetric point of view, the pregnancy was to all intents and purposes, normal and the pelvis adequate by the usual clinical methods of measurement. She had had one child 3 years previously. The labor lasted 24 hours and terminated in a spontaneous delivery; following the birth of the child, there occurred a retained placenta with a resulting mild postpartum sepsis. Further questioning revealed the fact that the patient, since her last pregnancy, suffered from edema occurring at times on various parts of her body. Because of this recurring edema, she was studied at that time by the Mt. Sinai Diagnostic Clinic and found to show sensitivity to numerous foods and articles. At her first visit to me, it was demonstrated that, although she had a patchy sort of edema of the face, hands, chest, legs and even the abdomen, nevertheless, her blood pressure was 104/60, her weight 148 (just prior to pregnancy, 139), her urine negative for sugar, albumin and microscopically. Since obviously this did not appear to be a toxemia of pregnancy, a tentative diagnosis of angioneurotic edema, generalized, was made. One and one-half grains of thyroid a day were given because of a known minus 18 basal metabolic rate. For the next two months under this regimen and although the edema did not improve, it became no worse. Her blood pressure remained low, the urine was negative, and her weight gain was only 5 pounds. Shortly after this, however, there was a sudden change in the entire picture. Within four weeks there was a gain of 9 pounds in weight, and the edema became more pronounced and persisted throughout the entire day and night. The blood pressure remained low (90 to 100 systolic and 40 to 60 diastolic), and the urine analysis negative. The patient, now 30 weeks pregnant, noticed that she was passing less and less urine. A carefully measured 24-hour specimen was only 550 c.c., and, although repeated for 1 week continuously, the amount voided remained in the neighborhood of 500 to 600 c.c. in 24 hours, with only one change: an increase in the specific gravity to 1.026 to 1.030. The edema at this time was massive and the patient hardly able to get out of bed. A combination of theobromine-sodium-salicylate gr. 4 and aminophyllin gr. 1½ every 4 hours by mouth was prescribed with the most amazing results. The patient began to void 3,000 to 3,500 c.c. daily for 4 days and then tapered down to 2,000 cubic centimeters. With this, part, but nowhere near all, the edema subsided. As soon as the medication was stopped the edema increased, and the amount of urine decreased to alarmingly small amounts. Throughout this period,

the fetus seemed to be progressing normally. Obviously, the medication was continued. On March 20, 1944, at 36 to 37 weeks' gestation, the patient developed lower abdominal pain which was assumed to be early and premature labor. Upon admission to Beth Israel Hospital, the pain stopped and, since there was no spotting or bleeding, and the cervix was closed with the membranes intact, she was sent home 18 hours later. No sooner did she arrive home when the pain began again. The pain was more or less continuous in the lower abdomen only, both over the uterus and in the flanks and not associated with nausea, vomiting or external bleeding. The uterus, although tender, was not board-like nor in fact had any rigidity at all. Morphine was required to ease the pain. Fortunately, on 3/22/44, some 48 hours after the pain began, she went into labor spontaneously and was fully dilated in three and one-half hours. The membranes ruptured spontaneously with a gush of frankly bloody amniotic fluid, and a few small dark blood clots. The head descended almost immediately, and a living male infant in good condition was delivered spontaneously. Immediately afterward, there was a gush of fresh and old blood and, by this time, it became increasingly obvious that we were dealing with a partial premature separation of a low implanted placenta. No difficulty was encountered with the placental delivery, and there was no postpartum bleeding. Examination of the placenta revealed no unusual macroscopic abnormalities. For the first 3 days post partum, the patient had no medication and again voided only 18 ounces, or 540 c.c. of urine daily. With the resumption of medication, voluminous amounts were passed again. The baby became excessively jaundiced some 36 hours after birth with no other symptoms, but vitamin K, minims x three times a day, was administered nevertheless. The most curious thing began 56 or so hours post partum: the baby had the same kind of patchy, almost brawny edema of the face, abdomen, legs, etc., that the mother had evidenced. The blood examination was more or less normal with 117 per cent hemoglobin and 5.8 million red blood cells with the usual configuration of white cells. The baby left the hospital 1½ ounces over birth weight with the jaundice almost gone, and the edema still present but less. At no time did the infant have a urinary shut down. The mother left the hospital in good condition with very little edema.

The explanation of the phenomena described might be predicated on what is known about angioneurotic edema. The kidneys shut down, the premature separation of the placenta and the edema which this patient demonstrated are all due to vascular spasm with diminution of blood flow and stasis. As far as the baby is concerned, it must be assumed that either the tendency to angioneurotic edema was inherited or the toxin, if there be one, was transported across the placenta. It is an observed fact that patients with mild allergy who become pregnant seem to lose most of their allergic manifestations; severe allergy or allergy of long standing seems not to be favorably affected by the pregnant state.

PREGNANCY NEAR TERM WITH PROLAPSE OF UTERUS

WILLIAM B. PATTERSON, M.D., PUUNENE, MAUI, T. H.

PROLAPSE of the uterus at or near term is rare. Kibel¹ recently reported a case and stated that 203 other cases had been reported in the literature. Complete procidentia at or near term is almost impossible, and the following case was only partial. My first thought was that there must be an abdominal pregnancy pushing the uterus down causing the procidentia.

Mrs. H. I., aged 28 years, gravida vi, para vi, reported for her first prenatal visit on March 16, 1944. Her last menstrual period was on August 21, 1943, and her expected date of confinement was May 28, 1944.

Her past medical history was negative. She had had five pregnancies with the delivery of six living female infants. The fifth pregnancy ended three weeks prematurely with the delivery of a five-pound infant who survived. She had also been admitted with false labor five weeks before term, during the fifth pregnancy. Her fourth pregnancy was twins, each of whom weighed four pounds, five ounces at birth. All of her other pregnancies had been normal, and none of the infants weighed as much as seven pounds at birth.

Physical examination showed a pregnancy of about six to seven months. There were a cystocele and a general relaxation of the pelvic floor. Otherwise, the examination was negative. The urine and blood Wassermann tests were negative. The blood pressure was 120/80.

The patient was next seen April 10, at 10 P.M., when she reported to the hospital with irregular labor pains. She stated that for the past four hours, a mass had been protruding from her vulva. She said that often during the past two weeks when she had done too much work this mass would protrude. She would lie down and gently replace it, and then take a short rest. On the day of admission, she had done the family laundry, and the vulvar mass again presented itself. This time, however, it became larger than before and she was unable to replace it. After three hours' time, she began having uterine pains and decided it was time to report to the hospital.

On admission, abdominal examination revealed a normal pregnancy of about seven months with vertex presentation. The fetal heart was 140 and of good quality. The uterine cervix was protruding through the vulva, and extended for six inches between the thighs. The cervix was swollen, edematous, and measured $2\frac{1}{2}$ inches in diameter at the tip. The tissue mass at the vulva was $3\frac{1}{2}$ inches in diameter. After sterile preparation, the cervix was gently compressed and replaced into the vagina. It returned easily and there was no tendency for it to recur with the patient lying down. The mucous plug was still in the cervix. To determine if there might be an abdominal pregnancy that had pushed the cervix down, I decided to introduce a finger into the cervix. The cervix easily admitted one finger, and the fetal head could be felt in the uterine cavity.

The patient was then given morphine sulfate, gr. $\frac{1}{6}$, and put to bed. The uterine pains disappeared and did not recur. She was kept flat in

bed for three days, and then allowed to get up. Vaginal examination at this time revealed the cervix to be normal and one finger dilated. The edema had disappeared.

On the fourth day, the patient was allowed to go home. She was told the nature of her condition and was instructed to rest in bed most of the time.

One week after discharge when she was to return for a prenatal visit, she returned in labor. Labor had started at 1 A.M., and was progressing normally. There had been no recurrence of the procidentia during the week at home. She delivered a male infant spontaneously in the L.O.A. position at 11 A.M. after 10 hours of labor. The placenta delivered spontaneously in five minutes by the Duncan mechanism. The infant weighed five pounds and six ounces, and appeared about one month premature. With breast milk it gained rapidly and was allowed to go home at the end of 10 days with the mother. The mother's course in the hospital was absolutely normal.

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ARRHENOBLASTOMA OF THE OVARY

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OF THE few ovarian tumors that exert endocrine influence upon the individual, the arrhenoblastoma by far presents the most colorful picture. It is also the rarest of the ovarian tumors, but in most cases the clinical findings are quite definite, and the diagnosis can usually be made preoperatively. To date, there have been approximately 60 such cases reported in medical literature. Long and Ziskind¹ reporting on 98 solid ovarian tumors from the New Orleans Charity Hospital in a ten-year period (1932 to 1941), found one case of arrhenoblastoma. My case was diagnosed during 1943 and it is indeed unusual, considering the rareness of the condition, for two such tumors to be found in the same institution within a period of 12 years. Perhaps as these authors suggest, further study of solid ovarian tumors, that in the past have simply been diagnosed as fibromas, may reveal the presence of an arrhenoblastoma or some other member of the special ovarian tumor group, such as granuloma-cell tumor, theca-cell tumor, Brenner tumor or dysgerminoma.

The four conditions that must always be differentiated are: cortical tumors of the adrenal, pituitary basophilic adenomas, adrenal cell rests of the ovary, and masculinizing luteomas of the ovary. In adrenal tumors, the breasts remain of normal size, and there is marked hirsutism. A tumor sometimes may be felt in the kidney region, and there may be other adrenal symptoms. In basophilic pituitary adenomas, the patients are usually obese and present other symptoms, such as severe headaches, referable to a pituitary lesion. Hirsutism is not a marked feature. Adrenal cell rests may be found sometimes in an ovary, and produce a tumor that exerts a masculinizing influence upon an individual similar to those with an arrhenoblastoma. Such a tumor is usually a highly malignant one, and the differentiation can be made only by microscopic examination. The ovarian masculinizing luteoma is considered by Schiller and Novak² to be really a tumor of adrenal tissue in most instances; therefore, a differentiation clinically would be a difficult, if not impossible, problem.

Most authorities report very little masculinization in tumors that are of the well-differentiated type, but this is not always true. The case which I am reporting showed marked masculinization, yet the microscopic picture is that of a well-differentiated type. Konte and Ragins³ report a case of the intermediate type in a patient aged 47, who six weeks after removal of both ovaries and uterus, showed return of the clitoris to normal size, and complete absence of hair on the chest. Boltuch⁴ reported a case of the undifferentiated type in a woman aged 28, who twelve days after removal of the involved ovary, showed a beginning resumption of normal voice, and complete return of menstruation on the twenty-sixth postoperative day, with normal breasts, and disappearance of abnormally placed hair.

Case Report

The patient (T-43, U.H. No. 81779, N. H., Gyn. Ward C 507), a young colored female, aged 24, was admitted to the hospital on February 20,

1943, with a chief complaint of cessation of menses and pain, and mass in the lower right quadrant.

The present illness dates back to eight years previously, when at the age of 15, she suddenly ceased menstruating. Menarche was at 11 years, with a regular cycle of thirty days, with a period of 3 days. The cessation of menses was sudden, and did not taper off. She went to see a physician, who gave her some medicine, and six months later she menstruated, but has not done so since. The patient noticed that her voice became harsher and deeper, the breasts became smaller, and there was an excessive growth of hair over the body. It was necessary for her to shave daily. She states that she did not lose any sexual urge.

The summer of 1942, she experienced a pain in the right lower quadrant with fever and slight nausea. She consulted a doctor in the country who sent her to Charity Hospital.

Patient was married at the age of twenty, with no pregnancies. The patient has for the last ten years drunk large quantities of water and has passed more than a gallon of urine (by measure) several times at night.

Recently, she has had some blurring of her vision, and frontal and parietal headaches. She suffers from hot flushes.

Physical Examination.—Blood pressure 132/100, temperature 98.8° F., pulse 80, respiration 18. There is a thick growth of hair on the upper lip, chin and throat. The thyroid is palpable. A large mass is felt in the lower abdomen measuring 10 by 7 centimeters. The mass is tender. The hair on the abdomen is masculine in distribution. The clitoris was enlarged to the size of the distal phalanx of the little finger. The cervix is infantile in type. The uterus was small and retroverted. The left ovary is prolapsed and enlarged, and a large mass is felt in the right adnexal region.

Laboratory Findings (2/22/43).—Red blood count 4,150,000, Hemoglobin 75 per cent, W.B.C. 6,000. Polymorphonuclear leucocytes 60 per cent, lymphocytes 19 per cent, monocytes, 19; eosinophiles 2 per cent. Urine negative on 2/23/43 and 3/4/43 B.M.R. on 2/23/43 was 26, and 2/26/43 11 per cent. X-ray of the skull on 2/23/43, lateral view, showed no evidence of erosion of the sella, abnormal convolutional markings or calcifications.

A preoperative diagnosis of arrhenoblastoma of the right ovary was made, and on February 27, the patient underwent a laparotomy. A supracervical hysterectomy, bilateral salpingo-oophorectomy and appendectomy was done; the left ovary being removed because it contained a tumor and the supracervical portion of the uterus being removed because both ovaries had to be. Her postoperative course was uneventful, and she was discharged on the twelfth postoperative day. Stilbestrol in dosage of 1 mg., three times daily, was started on the fourth postoperative day, and she was advised to continue this after leaving the hospital. However, she did not do this.

Pathological Report: Gross. The specimen consists of a uterus, both tubes and ovaries and a small portion of the cervix. The uterus measures 7.5 by 5 by 3 centimeters. The myometrium is 1 cm. in thickness. The endometrial cavity is normal in size, and the endometrium 1 mm. in thickness. On the left, the Fallopian tube is adherent to an ovarian mass measuring 4.5 cm. in diameter. Its external surface is smooth and grayish-white in color. Cut section of this tumor mass reveals a cavity 3 cm. in diameter, which is filled with a soft, yellowish grumous material, and also some black hairs.

The right ovary is composed of a mass 13 cm. in diameter. Its capsule is white and smooth, but scattered, here and there, under the capsule can be seen hemorrhagic areas of varying sizes. The surfaces exposed by cutting show somewhat of a soft heterogeneous surface composed of soft, yellowish areas varying in size from 1 to 4 centimeters. Scattered throughout are also nodular hemorrhagic areas of varying sizes. Both these nodular areas are separated by trabeculations of fibrous tissue. A few small cysts up to 1 cm. in diameter are scattered through the tumor. The right Fallopian tube is firmly adherent to the capsule and stretched.

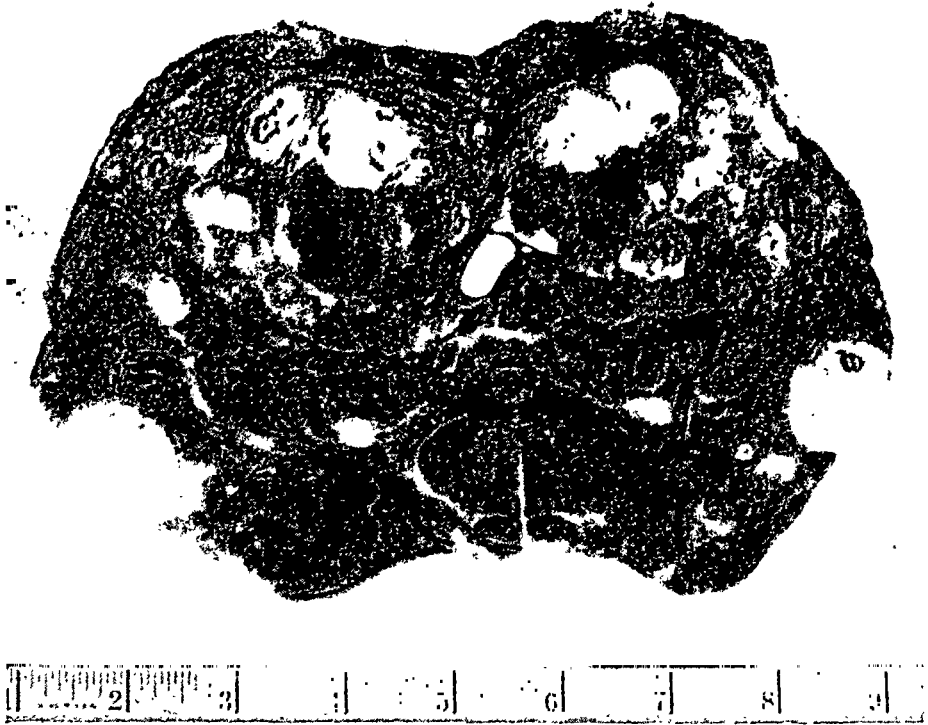


Fig. 1.—Arrhenoblastoma.

Microscopic. Section through both the tubes revealed a thickening of the wall with some degree of fibrosis. A number of plasma cells can be seen in the wall. Small areas of glandular formation, composed of mucosal tubal glands, can also be seen buried into the musculature. The membrane is flattened, and fibrosis can be seen in the stalks. The myometrium is normal. The endometrium is atrophic and shows early progestational changes.

The left ovary reveals numerous corpora amylacea. Dense areas of hyalinization are present, in which is embedded, here and there, calcareous material. In one area, groups of xanthomatous cells can be seen. In one area can be seen a cyst wall lined by a flattened epithelium.

The right ovarian tumor consists in the main of tubular-like structures with imperfect lumina. The cells composing these structures have large basally situated nuclei, the cytoplasm of which, more or less, streams into imperfect lumen. The nuclei are vesicular and the chromatin is gathered in clumps. The cytoplasm is eosinophilic and granular. Here and there, gathered in clumps throughout, are small areas of

interstitial cells. The interstitial and supporting tissue is made up of strands of well-formed connective tissue. In certain areas, there is necrosis and hemorrhage. Occasionally, one sees, in small areas, neoplastic cells which have lost their polarity, and are scattered as single or small nests of cells in the interstices of the connective tissue.

The diagnosis was bilateral salpingitis, left ovarian dermoid cyst, atrophic progestational endometrium and arrhenoblastoma of the right ovary of adult type.

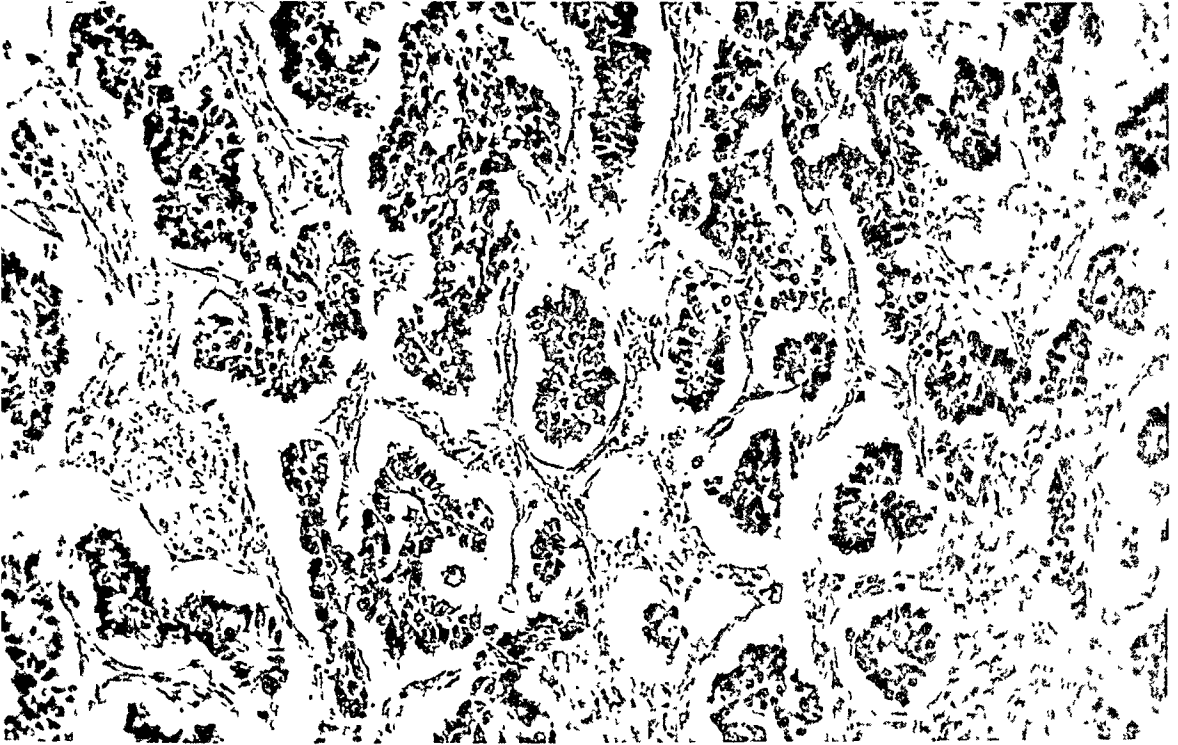


Fig. 2.—Microscopic section of arrhenoblastoma. Shows a characteristic portion of the tumor of the right ovary. Imperfect tubules with basal nuclei are prominent. These are separated by a supporting framework of connective tissue. The structure is that of an adult arrhenoblastoma.

Summary

Before operation on February 27, 1943:

1. Abrupt cessation of menses at 15.
 2. Onset of masculinizing traits at this time (deepening of voice, appearance of hair, a beard, masculine physique, atrophy of breast. Progressive increase in sex desire, hypertrophy of clitoris (all progressive from 15 to time of admission at 24).
 3. Had pain in lower abdomen, headaches.
 4. Right abdominal mass found.
 5. Marked hypertrophy of muscles of shoulders and upper extremities.
- Since leaving hospital:
1. Hot flushes 3 to 6 daily.
 2. Night sweats.
 3. Decrease in number and intensity of headaches.
 4. Marked increase in size of breasts.
 5. Loss of much hair on abdomen, back, arms and legs. Still has beard, shaves twice a week, not so thick, and does not grow as fast.
 6. Decreased libido.

7. No change in voice.
8. Gain of 22 pounds.
9. Some decrease of clitoris enlargement.
10. Muscles of upper extremity almost same.
11. Chest plate negative for metastatic lesion.

She was again put on stilbestrol in dosages of one mg., three times daily, and advised to continue this drug until seen again. Her general health was excellent, and she seemed quite satisfied with the results obtained following the removal of the pelvic organs.

Conclusions

A proved case of an arrhenoblastoma of the ovary in a 24-year-old colored female has been reported, with a follow-up nine months after removal of the tumor. Microscopic examination showed it to be of the adult or well-differentiated type. Following its removal, the patient became more feminine, but still retains some of the male characteristics that had developed in her at age 16. She retained her deepened voice, the clitoris remained somewhat larger than normal and the muscles of the upper extremity showed little change. She also reported that she still grew a beard that required shaving, but much less than before surgery. It is hoped that in time, most of these male characteristics will continue to diminish. The finding of an early progesterational endometrium was, indeed, interesting and rather difficult to explain. The presence of a dermoid cyst in the opposite ovary offers additional circumstantial evidence in support of the theory of teratomatous origin of the ovarian arrhenoblastoma.

I wish to acknowledge and also to thank Dr. Bjarne Pearson of the Department of Pathology, Tulane University, for his excellent description of the tumor.

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210 BARONNE STREET

REDUCTION OF AN INVERTED UTERUS FOLLOWING INTRA-VAGINAL PACKING

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(From the Obstetrical Service of Morrisania City Hospital)

THIS case of inversion of a puerperal uterus is presented for its unusual feature—complete reduction following intravaginal packing. One other similar case was found, described by Harer and Sharkey.¹ In their case, the condition was diagnosed as a pedunculated fibroid, and a laparotomy was done with hysterectomy. When the peritoneal cavity was opened, it was found that the uterus, which had actually been inverted, had been replaced in the process of packing the vagina before operation. On examination of the excised uterus, no fibroid was found.

Case Report

Our patient was a 23-year-old white female, para ii, gravida ii, who was admitted to the Morrisania City Hospital at 3:30 A.M. on October 3, 1943, with vaginal bleeding as her chief complaint.

Her first delivery had been spontaneous and uneventful. The past medical and surgical histories were essentially negative.

During her present pregnancy, she had received prenatal care from a midwife. She had a normal spontaneous delivery of a full-term 6¼-pound female baby at home about 8:45 P.M. on October 2, 1943. About 45 minutes after the delivery of the baby, a local physician was called by the midwife because she noticed a mass protruding from the vagina with the placenta attached. The physician, on arrival, found the uterus inverted with the placenta attached lying in a wash basin. The woman's condition at this time was good. He manually removed the placenta from the uterus, and then pushed the fundus into the vagina. He thought that he had completely replaced the uterus. At 2:15 A.M., 4½ hours following delivery of the baby, the physician was recalled because the patient was bleeding. He found her in shock and bleeding. Her blood pressure was 70/40 and hemoglobin 40 per cent (Sahli). She was given an infusion of 1,000 c.c. of 5 per cent glucose, 1 c.c. of adrenalin and 1 c.c. of obstetrical pituitrin before being sent to the hospital.

Examination on admission revealed the patient in moderate shock, and bleeding moderately. Her pulse was 140 and blood pressure 80/40. Since the diagnosis of inversion was not made by the resident, he gave her ½₃₂₀ grain of ergotrate and 1 c.c. of obstetrical pituitrin intramuscularly soon after admission. This was followed by a transfusion of 500 c.c. of bank blood. At 5:30 A.M. an abdominal examination revealed the fundus to be firm, 4 fingers below the umbilicus, and although no definite cupping was palpated, the fundus was not well rounded. She lost about 500 c.c. of blood from the time of admission to the time she was taken to the operating room (2¾ hours). Her general condition remained about the same. At 6:15 A.M. or 9¼ hours post partum, the

patient was anesthetized in order to make a definite diagnosis and to check the bleeding. Examination disclosed an inversion of the uterus with about 3 inches of the firm fundus below the cervix. At this time, while the abdomen was well relaxed, bimanual examination revealed a definite cupping of the fundus. Simple palpation of the inverted uterus caused a marked increase in vaginal bleeding. The vagina was then packed with 25 yards of iodoform gauze, especially placed against the inverted uterus to control bleeding. No difficulty was found in inserting this large amount of gauze. The patient's condition remained about the same during this manipulation as noted by the blood pressure reading of 60/30 before anesthesia was begun, and 70/40 at the end of the procedure. Packing of the vagina checked the bleeding. The patient's condition improved almost immediately. Abdominal examination 4 hours later, disclosed the uterus slightly cupped and displaced under the left costal border by the pack in the vagina. A second examination 12 hours after the packing, revealed a well-rounded fundus with the inversion completely reduced (Fig. 1). She was given two more

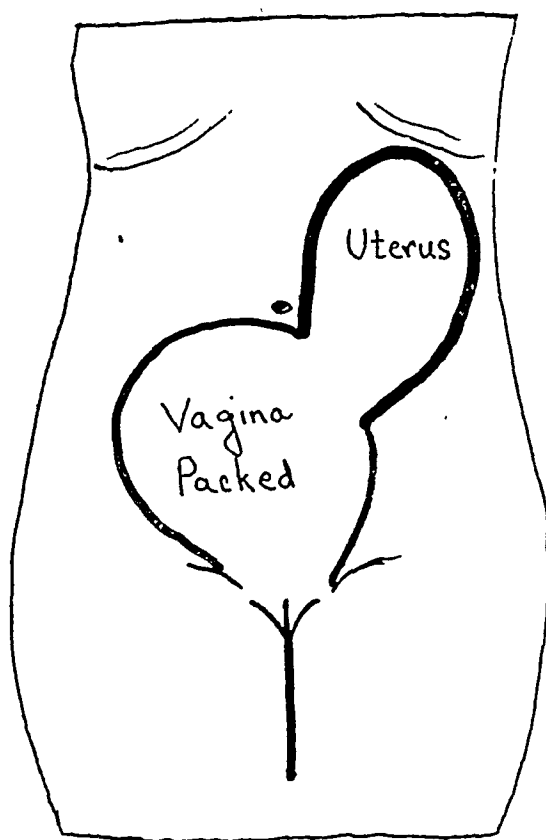


Fig. 1.

500 c.c. transfusions of bank blood and placed on sulfathiazole therapy for five days. Fifty-six hours after the packing, the vaginal iodoform gauze was removed under a general anesthesia. The inversion was found completely reduced, with the fundus convex in contour. Two fingers were introduced into the uterine cavity to be sure that a partial inversion above the cervix did not remain. The distended vagina disappeared following removal of the packing. The patient made an uneventful recovery, except for a rise in temperature to 102° F. just before she

signed herself out contrary to advise on the ninth day post partum. The uterus was well involuted, and there was no evidence of uterine prolapse. The family physician reported that her temperature came down to normal on the second day at home.

Discussion

Since nothing is known about the conduct of the third stage in this particular patient, it would be very difficult to state definitely the cause of the inversion of the uterus.

The treatment of this patient was conservative because she was in shock, and because slight vaginal manipulation caused a marked increase in the vaginal bleeding. Of late,^{1, 2} there has been an increased trend to make no attempt to replace an inverted uterus when the patient is in shock. The mortality figures have been found to be lower, if reduction of the inversion either by taxis or operative means is attempted after the patient has responded to shock therapy.

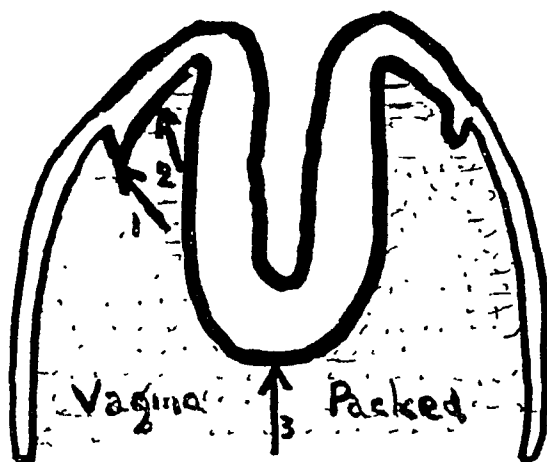


Fig. 2.

Although the rounded fundus was not palpated until 12 hours after the vagina was packed, the uterine replacement probably began during and as a result of the packing. The cessation of the vaginal bleeding, and the immediate and marked improvement in the patient's general condition following the packing are in favor of this opinion. The possible explanation of how the packing reduced the inversion may be noted in Fig. 2. The overdilatation of the vaginal vault with packing caused the constricting cervix (arrow 1) to dilate and, therefore, removed the ring gripping the fundus. The dilatation of the constricting ring is the most important step in the reduction of an inverted uterus by taxis, also the packing caused pressure against the uterine wall just above the cervix (arrow 2). This technique corresponds to the procedure used in manual reduction of this condition. Finally, pressure exerted by the packing against the fundus further influenced the replacement of this organ (arrow 3).

The authors would like to suggest that where vaginal packing is indicated in the treatment of an inverted uterus, a large amount of packing be employed. Since this condition is very rare and an obstetrician does not encounter more than a few cases during his entire experience, it would be very difficult for any individual investigator to evaluate this form of treatment. However, if success in similar cases were to be ob-

tained by others, the use of a large amount of intravaginal packing would emerge as another form of treatment of a very grave complication in obstetrics.

The authors wish to acknowledge the very helpful assistance of Dr. Milton J. Goodfriend in the preparation of this paper.

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1749 GRAND CONCOURSE

1882 GRAND CONCOURSE

Department of Statistics

ABDOMINAL CESAREAN SECTION AT THE CLEVELAND MATERNITY HOSPITAL

W. R. BARNEY, M.D., F.A.C.S., CAPTAIN JOHN S. FISH, M.C., A.U.S.,
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THIS report deals with the obstetric cases delivered by abdominal cesarean section from the years 1931 to 1941. It comprises an analysis of 1,317 such operations, thus permitting a rather thorough study of certain phases of the subject. The cases included are from both the staff and private services.

Incidence.—A true picture of the incidence of abdominal cesarean section on our service is probably not strictly obtainable. Due to the character of the staff, many women in need of section are referred directly to the maternity division for this operation by physicians who do not have privileges allowing them to deliver their normal material here.

The staff service is a part of the maternity district obstetric service. Normal multiparas are delivered in their homes. Primiparous patients and operative cases are cared for at Maternity Hospital or on the obstetric service of Cleveland City Hospital, both of which are under the direction of Dr. Arthur H. Bill and the Western Reserve University School of Medicine.

It is necessary, then, to include the figures from all of these services to obtain a true section incidence (see Table I). This figure is further influenced by the fact that many cases in need of operative delivery are referred directly to City Hospital by general practitioners doing home deliveries among the financially poorer groups of our city.

TABLE I. TOTAL DELIVERIES AND CESAREAN SECTIONS 1931 TO 1941

| | DELIVERIES | SECTIONS |
|----------------------------|------------|----------|
| Cleveland City Hospital | 5,429 | 299 |
| Maternity Hospital—Private | 12,683 | 776 |
| Maternity Hospital—Staff | 9,592 | 667 |
| Maternity District | 19,717 | |

We have performed 776 private and 668 staff sections at Maternity Hospital, and another 299 at Cleveland City Hospital during this period. Our incidence is 1,743 sections in 58,830 deliveries at Maternity Hospital, on the Maternity home delivery service and at Cleveland City Hospital. The incidence is therefore, 2.9 per cent. The incidence among cases delivered exclusively at Maternity Hospital is 1,444 sections in 23,396 deliveries or 6.1 per cent. The private incidence is 6.0 per cent while that of the staff service is 6.3 per cent. We have abstracted 1,317 of these cases.

Type of Patient.—This series of 1,317 cases contained 596 staff patients, and 721 private patients. Most of the private patients were white and almost all of the colored patients were found upon the staff service. There were 1,043 white and 274 colored patients. The colored percentage is up paralleling that of the sections themselves—there being 16 colored sections in 1932, and 53 in 1941.

Mortality and Morbidity.—There were 24 maternal deaths in the series. This is a mortality rate of 1.7 per cent. The causes of death are listed in Table II. The mortality varied with the type of section as follows: laparotrachelotomy 0.9 per cent, classical 2.6 per cent, Porro 6.1 per cent and extraperitoneal no deaths. The private mortality was 0.5 per cent while that of the staff service amounted to 3.3 per cent.

TABLE II. CAUSES OF MATERNAL DEATH FOLLOWING CESAREAN SECTION

| | CASES |
|-----------------------------------|-------|
| Bronchopneumonia | 9 |
| Postoperative shock (eclamptic) | 6 |
| Pulmonary embolism | 2 |
| Postoperative shock (separation) | 1 |
| Generalized septicemia | 1 |
| Acute cardiac dilatation | 1 |
| Postpartum hemorrhage | 1 |
| Rheumatic heart disease (failure) | 1 |
| Peritonitis | 1 |
| Chronic pyelonephritis | 1 |

Morbidity, figured as temperature of 38.0° or over for two or more consecutive days, was found in 594 cases or 45 per cent. This morbidity will be further analyzed later in this paper. The staff morbidity was 54 per cent as contrasted with the private morbidity of 37 per cent. The morbidity among white patients was 41 per cent, while that of the colored group amounted to 60 per cent.

Indications for Section.—The indications for section will be found tabulated in Table III.

TABLE III. INDICATIONS FOR ABDOMINAL CESAREAN SECTION

| | CASES | PER CENT |
|--------------------------|-------|----------|
| Repeat section | 404 | 30.1 |
| Small measurements, etc. | 354 | 26.8 |
| Placenta previa | 120 | 9.1 |
| Premature separation | 102 | 7.7 |
| Toxemia | 101 | 7.6 |
| Cervical dystocia | 64 | 4.8 |
| Medical indications | 59 | 4.4 |
| Pelvic tumor | 38 | 2.8 |
| Unclassified | 70 | 5.3 |

Types of Section Done.—These 1,317 sections were divided as follows: classical 40 per cent, laparotrachelotomy 55 per cent, Porro 3 per cent and extraperitoneal 1 per cent. Among the classical sections, there were 100 high and 430 low sections. The laparotrachelotomies were divided as follows: transverse 702, and vertical 23. Eleven of the classical sections and four of the laparotrachelotomies were followed by hysterectomy.

Our morbidity declined about 20 per cent between the years 1934 and 1941. During this time, the percentage of laparotrachelotomies was

more than doubled. In general, then, it may be said that morbidity declined as the low-flap operation was employed more often.

What Procedures Affect the Morbidity.—It seemed interesting to attempt to find out what affected the morbidity rate in abdominal cesarean section. Several possible factors were, therefore, investigated. First of all, what was the effect of extra surgery? Further surgical procedures such as tubal resection, myomectomy, cornual resection, etc., were done in 253 cases. Of these, 39 per cent showed a morbidity. This is somewhat less than the total morbidity.

In 1,230 cases the membranes were intact, and in 90 they were ruptured. The cases with ruptured membranes showed a 60 per cent morbidity as contrasted with 45 per cent morbidity for the entire series.

The cervix was not dilated in 988 cases, and 38 per cent of these showed a morbidity. In the cases showing one to three fingers' dilatation at the time of section, 56 per cent showed a postoperative morbidity, while 66 per cent of those over three fingers dilated were morbid.

In the cases of premature separation of the placenta, the morbidity was 59 per cent, while the group sectioned for placenta previa ran a 51 per cent morbidity.

The effect of anemia is shown by the fact that the cases with a hemoglobin of 60 per cent or less, had a morbidity of 75 per cent. The cases with a hemoglobin of between 60 and 75 per cent showed a morbidity of 57 per cent, while with a rise of the hemoglobin to 75 per cent or over, the morbidity fell to 47 per cent. These figures would be even more striking had hemoglobin determinations been carried out routinely on the private service rather than just on those patients whose condition specifically warranted it.

Morbidity increased with the number of rectal examinations. Morbidity due to some form of pelvic infection appeared in 1.9 per cent of those in whom no rectal examinations were done, while it increased to 13 per cent in those who had three or more rectal examinations. Pre-operative vaginal examinations resulted in a morbidity due to pelvic infections in 20 per cent of the cases. It must be remembered in evaluating these data, that rectal and vaginal examinations are done most frequently in those cases where a potential morbidity already exists.

Those cases which had a trial of labor showed a morbidity of 54 per cent, while there was a morbidity of only 41 per cent among the elective sections.

The effect of operating an anesthetic time is shown in Tables IV and V. In general, the longer the operating or anesthetic time, the greater the morbidity.

TABLE IV. TIME OF ANESTHESIA AND MORBIDITY

| MINUTES | CASES | MORBID CASES | PER CENT MORBIDITY |
|----------|-------|--------------|--------------------|
| 20 to 30 | 45 | 8 | 17 |
| 30 to 40 | 145 | 64 | 44 |
| 40 to 50 | 226 | 98 | 43 |
| 50 to 60 | 420 | 188 | 42 |
| 60 to 90 | 396 | 182 | 46 |
| Over 90 | 57 | 33 | 57 |

Those cases requiring postoperative catheterization showed a morbidity due to genitourinary tract causes of 15 per cent. This corresponds closely to the figure of 13 per cent genitourinary morbidity in

TABLE V. TIME OF OPERATION AND MORBIDITY

| MINUTES | CASES | MORBID CASES | PER CENT MORBIDITY |
|----------|-------|--------------|--------------------|
| 20 to 30 | 212 | 79 | 38 |
| 30 to 40 | 388 | 153 | 39 |
| 40 to 50 | 327 | 147 | 44 |
| 50 to 60 | 274 | 130 | 46 |
| 60 to 90 | 108 | 63 | 58 |
| Over 90 | 8 | 5 | 62 |

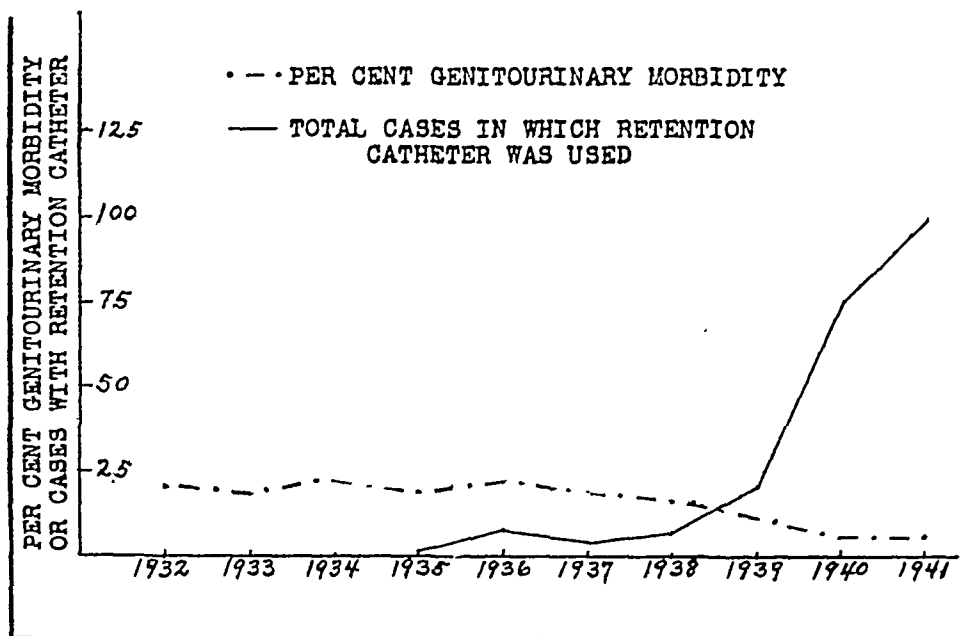


Fig. 1.—The effect of the use of the retention catheter on the urinary morbidity.

the whole series, and also to that obtained in a series of cases including all types of deliveries recently studied here. Those cases in which a postoperative retention catheter was used, however, showed a genitourinary morbidity of only 4 per cent. In Fig. 1 the effect of the use of the retention catheter is shown graphically.

Laparotrachelotomies required catheterization 31 per cent of the time, classical sections 26 per cent. Cases in which a retention catheter was used are not included in these figures.

The causes of morbidity are listed in Table VI.

TABLE VI. CAUSES OF MORBIDITY

| | CASES | PER CENT |
|---------------------------|-------|----------|
| Genitourinary tract | 173 | 13 |
| Abdominal wound infection | 93 | 6 |
| Pelvic infections | 73 | 5 |
| Operative reaction | 67 | 5 |
| Respiratory tract | 44 | 3 |
| Retained lochia | 20 | 1 |
| Phlebitis | 16 | 1 |
| Unknown | 89 | 6 |
| Unclassified | 50 | 3 |

Other Considerations.—Slightly more than half of these cases of small measurements and cephalopelvic disproportion were allowed to

have a trial of labor. The balance was operated upon as elective sections. Laparotrachelotomy was used twice as often upon patients already in labor, while the low-flap type of operation and classical section were done equally as often upon patients not in labor.

The most popular type of premedication was amytal and atropine, while amytal alone was a close second. A large number of the cases in labor was already started upon morphine and scopolamine routine at the time of section.

Summary

A series of 1,317 cases of abdominal cesarean section operated upon between the years 1932 and 1941 has been studied. This study included mortality and morbidity, the causes of morbidity and other considerations.

Correspondence

Cesarean Section

To the Editor:

The report by Rosensohn, Kushner and Wahrsinger titled "Cesarean Section at the Bronx Hospital" (AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, August, 1944, pp. 274-277) prompts this communication.

There are several altogether remarkable facets in their report, the most outstanding being the obvious and total failure of an artificial obstetric oligarchy in its attempt at reducing mortality following cesarean section. Stimulated, apparently, by the Academy of Medicine report on maternal mortality and by figures obtained from the Hospital Information Bureau, the authorities at the hospital set out to reduce the incidence and mortality of cesarean section. This was to be done by limiting the number of men privileged to do the operation and by consultation which, "did not need to be direct." If such consultation bears any resemblance to what the authors described as "telephone permission" in an emergency, then it probably is as valueless as telephone consultation. Obstetric consultation by telephone is invalid and futile. The consultant must accept the interpretation of signs, symptoms and a dynamic situation as verbally conveyed to him by the man on the scene who may or may not be accurate, and who may or may not be ignorant. The consultant himself, awakened from a sound sleep or disturbed at his own work can scarcely possess the intellectual clarity required to analyze a complex situation of which his knowledge is merely a verbal communication. Telephone consultation may have a certain "beauty" in a hospital record. Its practical value is *nil*. Obstetrics is still a clinical art.

The plan of the Bronx Hospital (and there is nothing in the report to indicate success or failure in the reduction of incidence) was dangerous from at least one viewpoint. It fixed responsibility for the results of cesarean section squarely upon the shoulders of a little group of obstetricians and gynecologists. From the day the plan was instituted, they could no longer lay the blame for section mortalities at the thresholds of, "surgeons, dermatologists, nose and throat specialists, and orthopedists." (And one is forced to wonder why obstetricians eternally insist that surgeons cannot perform cesarean section. What obstetrician possesses the technical skill or the familiarity with the abdomen as a surgical field possessed by the average surgeon?) Having fixed responsibility, presumably upon qualified obstetricians, at the end of a ten-year period there is reported a maternal mortality of 3.2 per cent. Is this remarkable? Is this the fruit of noble experiment? Is it sufficiently superior to what the, "surgeons, dermatologists, nose and throat specialists and orthopedists" might have done? Would such men (it is incredible that their minds are as rigid as obstetric minds) in a time when the whole obstetric literature has fairly screamed the infinite superiority of the low segment sections have done *255 classical sections* out of a total of 494? Certainly obstetricians might have set a better example. In progressive action and thought classical section would be limited to 5 cases in 494 and those would be in the rare instances in which the operator is unable to reach the lower segment because of intra-abdominal adhesions or where he chases to avoid the lower segment because of a low-lying placenta. And even this latter is no valid excuse for the employment of an inferior and outmoded technique.

Citing McLane and Kuder, the authors venture a discussion of the problem of vaginal delivery in pregnancies subsequent to cesarean section. "These studies would indicate that the fact that a cesarean had been performed at one time does not preclude the possibility of a vaginal delivery in a subsequent pregnancy but *the fear of a rupture of the uterus must be kept constantly in mind, and the patients watched with utmost care during their pregnancy and labor.*" Again, "Also, in cases of former cesarean section, the obstetrician may have the courage to permit vaginal delivery. . . ." The hackneyed, "once a section, always a section" is no axiom. Even those who hold it as such do not maintain that one section precludes subsequent vaginal delivery. The expression is more a colloquialism which handily explains a factual situation; it means that the possibility of rupture of the uterine scar in labor must be reckoned with. Four in one hundred classical scars rupture.

One in four hundred lower segment scars ruptures. To permit labor is a gamble. There is no question that the odds greatly favor the patient but the element of chance still exists. Watching patients "with utmost care" is an excellent brand of nonsense since the only thing to watch for is the actual rupture of the uterus. The diagnosis of impending rupture is a great rarity. If, under exquisite observation, the rupture occurs in a well-equipped maternity where, within a few minutes the operator can open the abdomen and repair the damage, then disaster may be averted. If the rupture occurs with the patient at home, then rupture is synonymous with death. Counter to the crippling fear of uterine rupture is the elective section two weeks before term.

In the management of the pregnancy and labor subsequent to section, it is not the obstetrician who must be courageous. It takes courage to be the patient. The obstetrician risks little; "bubble reputation," the annoyance of explaining mortality at a staff conference and the few hours of sleep stolen, perhaps, by a troubled conscience. *The patient risks life.* It is not for the obstetrician to dictate management on the basis of academic or didactic reason or the statistic experience in fanciful obstetric writings. It is his duty to explain adequately to his patient and her responsible relatives the problem of scar rupture and to permit them freely to make the choice of procedure. How many patients will risk their lives over the questionable integrity of an unseen scar? How many patients will accept even the one chance in four hundred? Is it the happy sound of the words "watched with utmost care" that accounts for their use? Why are we not told what to watch for? What is there to watch for? What is there in prenatal care which predicts the character of fibrous tissue in the uterine scar? What is there to predict the reaction of such tissue under the stress of powerful myometrial contraction?

On page 277 the authors venture this: "the cesarean operation is not to be regarded as a panacea for all types of labor. . . ." What is this creation? What *obstetrician* has ever maintained the preposterous proposition that section is a panacea? What obstetrician has ever denied the risk and mortality attached to section? But there are obstetricians who know that the mortality of *elective lower segment section* is less than 1 per cent, and that the classical section was an excellent procedure . . . in 1882.

"The striking features of this report from the Bronx Hospital are first, the high maternal and fetal mortality, and second, the low incidence of the operation." But one must note that the incidence of section in private cases is at least double that in ward cases. Does this arouse curiosity? There need be no searching inquiry. The plain fact is that plans of management may be freely applied to ward cases (and daily they are applied and in maternities that would warrant the roaring applause of conservatism) which the obstetrician would never dare inflict upon his private cases.

Whether or not low incidence of section is salutary is a moot point. To deliberately set out to reduce section incidence is a procedure bearing unpleasant implications. The immediate question would naturally be, "What was going on before the crusade began?" Is it possible that concentration on a superior technique might make for a happier statistic picture regardless of incidence? Is it possible that obligatory consultation (?) is a form of meddlesome midwifery? Is a major weapon in the obstetric armamentarium such an evil that the energies of a staff must be directed toward limiting its use? Of what value is the opinion of the consultant whose avowed purpose is a reduction of the incidence of the operation? Reduction of incidence being the goal then the first thought of the consultant, if he holds to his conviction, will be, "How can I avoid section?" rather than, "Is section indicated?" Often enough, this thought alone will mean long tests of labor, bagging placenta previa and risking the priceless babies of elderly primigravida. It will mean too, that cases will come to section after the incomparable values of the elective period are lost.

"We feel that the incidence of cesarean section can still further be reduced." In the face of the reported mortality, the facetious might well produce a very obvious retort to such a statement. In another vein, it is no impertinence to ask, where resides the obstetric worth of the original plan? Where is there wonder in it?

FRED A. KASSEBOHM, M.D., F.A.C.S.
MILTON J. SCHREIBER, M.D., F.A.C.S.

NEW YORK, N. Y.
AUGUST 26, 1944

The Use of the South African Frog Pregnancy Test

To the Editor:

Our attention has been drawn to the increasing publicity given in the lay as well as the scientific press in the United States to the use of the South African frog (*Xenopus laevis*) as a test for pregnancy.

In all these recent communications, there has been no adequate reference to our original report published in October, 1933, in the *Proceedings of the Royal Society of South Africa*.

In the interests of accuracy, we feel it necessary to point out that this test is not being described for the first time, as it is already nearly 11 years old.

Because we feel sure that our American colleagues who are using the frog test have no desire to create confusion about the priority and authorship of this test, we have felt it necessary to draw attention to the correct citation of the original reference.

The interested reader will find subsequent references in: *Nature* 133: 762, 1934; *South African M. J.* 9: 202, 1935, i.e., some 3 years before Elkan first used the test in England, and about 7 or 8 years before Weisman et al. first used the test in America.

The most recent review of the test, summarizing 10 years' experience in this field, will be found in: *Clinical Proceedings* 3: 186, 1944.

H. A. SHAPIRO.

H. ZWARENSTEIN.

CAPE TOWN, SOUTH AFRICA,
AUGUST 17, 1944.

To the Editor:

Several years ago a subcommittee of the American Committee on Maternal Welfare succeeded in classifying toxemias of pregnancy. Hyperemesis gravidarum and acute yellow atrophy of the liver were included, although most of the committee believed that the term of "toxemia" should be restricted to those patients having hypertension, edema or proteinuria. This classification has been accepted by most clinics in the United States.

If patients are adequately followed during pregnancy and for six months after delivery, the correct diagnosis can be made in most instances. In a recent study of 348 patients, who had a toxemia in the first pregnancy on our service, and had a subsequent delivery on our service, the diagnosis of hypertensive disease was incorrect in 8 per cent since the following pregnancy was normal. Presumably, an incorrect diagnosis was made in 21 per cent because these patients were diagnosed pre-eclampsia in the first pregnancy and had a recurrence of toxemia in the next. It is possible that they did have pre-eclampsia, or that they had a combination of pre-eclampsia and hypertensive disease.

Dr. Titus has recently suggested another classification claiming that the previous one was at fault. (June, 1944, issue, page 817.) I believe a longer use of the generally accepted classification, together with a longer follow-up, will demonstrate that the classification is a good one providing it is restricted as described above.

WILLIAM J. DIECKMANN, M.D.

CHICAGO, ILL.
SEPTEMBER 27, 1944.

Department of Reviews and Abstracts

Selected Abstracts

Gynecologic Operations

De Moraes, A.: Vaginal Hysterectomy After the Menopause for Nonmalignant Conditions, *An. brasil. de ginec.* 8: 209-217, 1943.

The author reports a series of vaginal hysterectomies performed during the menopause and afterward for nonmalignant conditions. The majority of women had abnormal uterine bleeding. In most of the cases, disturbances were found, chiefly prolapse of the uterus, cervical erosions, chronic cervicitis, chronic endometritis, endometrial hyperplasia and fibroids. The author believes that vaginal hysterectomy, done under local anesthesia, which is the routine in his clinic, is indicated when these abnormalities are found in a functionless uterus. The reason is that these pathologic conditions are potentially malignant. The operation is therefore prophylactic treatment against cancer.

J. P. GREENHILL.

Frete, F. R.: Treatment of Prolapse of the Uterus by the Halban Operation, *An. Inst. de Mat. y Asist. Soc.* 4: 131-147, 1942.

After reviewing various operations for prolapse of the uterus such as the Neugebauer, Le Fort, Wertheim-Schauta, Watkins, Kahr, Donald, etc., the author expresses his preference for the Fothergill and Halban operations. Among 52 cases of prolapse treated by the Halban operation, there were no deaths and only insignificant complications. The author considers this operation to be simple, rational and anatomic, and one which can be used in any degree of prolapse.

J. P. GREENHILL.

De Vasconcellos, E. P.: Some Considerations of Prolapse of the Uterus, *An. brasil. de ginec.* 8: 197-208, 1943.

During the last five years 216 women were admitted to the author's gynecologic clinic and of this number 55 had prolapse of the uterus, an incidence of 2.54 per cent. Of the 55 women 16 had first degree, 16 had second degree and 23 had third degree prolapse. The most frequent operations performed among the 45 women were the Halban (15 times), total vaginal hysterectomy (11 times), and the Fothergill operation (8 times). General anesthesia was used 17 times, local anesthesia was used 26 times, and spinal anesthesia twice. There were 4 recurrences in this series of cases. The author favors the Mayo vaginal hysterectomy in postmenopausal women.

J. P. GREENHILL.

Fox, E. A.: Implantation of Endometrium as Complement to Hysterectomy for Uterine Myomas, *Obst. y ginec. Latino-Am.* 1: 561-567, 1943.

In order to maintain the functional relationship between the uterus and the ovaries the author implants a large piece of endometrium. He used this procedure in 16 cases. The technique is as follows: after removing the fibroid uterus, a piece

of endometrium about 2 cm. wide is stripped from the uterine fundus and placed directly on the cervical incision. Special attention is paid to inserting the endometrial flap over the internal os. The endometrial tissue is sewed in place by interrupted catgut sutures and then the wound is peritonealized as usual. The results are encouraging. Menstruation, though not profuse, reappeared sooner or later and persisted in all the women. Symptoms of the menopause appeared only in 3 patients.

J. P. GREENHILL.

Meigs, Joe Vincent: Carcinoma of the Cervix—The Wertheim Operation, Surg., Gynec. & Obst. 78: 195, Feb., 1944.

Forty-seven cases of carcinoma of the cervix were treated by Wertheim operation plus Taussig dissection of the pelvic lymph nodes with an immediate operative mortality of 0 per cent. Seventeen per cent of these showed lymph node involvement, and 6 of the patients had received treatment elsewhere, the carcinoma having recurred. Insufficient time elapsed for any conclusion to be drawn as to the comparative effectiveness of the method of treatment. It is the author's belief, however, that this method of treatment will give better end results than the present methods of irradiation. Urethral injury is the greatest drawback to the operative procedure.

L. M. HELLMAN, LT. (M.C.) USNR.

Newborn

McCall, A. J., Race, R. R., and Taylor, G. L.: Rhesus Antibody in Rh-Positive Mother Causing Hemolytic Disease of Newborn Infant, Lancet 246: 214, 1944.

The authors describe a case of hemolytic disease of the newborn infant where the mother was Rh-positive and had in her serum an antibody similar to, but not identical with, anti-Rh such as was first described by Levine, et al. The writers term their serum St. It has been found to react with blood of 80 per cent of people including all the Rh-negatives, all the heterozygotes (Rh_h) and some of the homozygotes Rh-positives (RhRh). By using St and other forms of anti-Rh sera, it has proved possible to determine serologically the genotype of about 80 per cent of people.

The authors present an interesting account of the family history and blood groups in the three sons and parents.

The article is valuable original source data for interesting readers on the problems of heterospecific serum and blood factor differences of pregnancy as correlated to causes of fetal death. In this case the infant was saved by two transfusions from one of the St-negative group-O donors.

CLAIR E. FOLSOME.

Park, L. M.: Large Twins, Lancet 246: 118, 1944.

Park reports an unusual obstetrical case. The patient, aged 30, para iv, gravida vi, was delivered by classical cesarean section of a set of large twins. The combined weight of the twins was 19 pounds, 2 ounces (8,705 Gm.), the individual weights being 10 pounds, 14 ounces (4,956 Gm.) and 8 pounds, 4 ounces (3,749 Gm.).

The classical section was performed sixteen hours after premature rupture of the membranes, before the onset of labor. Previous roentgenographic study revealed the fetuses lying longitudinally, a breech and a cephalic presentation respectively. The placental weights totaled 3 pounds, 11 ounces; or 2 pounds, 2 ounces, and 1 pound, 9 ounces respectively. The patient experienced excessive post-partum bleeding which required a blood transfusion. Otherwise the convalescence of the mother was uneventful.

A literature search by Park suggests that the larger of these twins is the heavier so far credibly reported.

CLAIR E. FOLSOME.

Darke, Roy A.: Late Effects of Severe Asphyxia Neonatorum, *J. Pediat.* 24: 148, 1944.

Asphyxia neonatorum is a clinical term commonly used to designate the manifestations of anoxia which results from obstruction to placental or fetal circulation, obstruction to fetal respiratory passages, narcosis, prematurity, abnormal delivery trauma, maternal anemia, maternal fever, rapid labor, instrumental delivery, long second-stage labor or premature rupture of membranes.

The author reviewed 25,261 deliveries (New York Hospital, 13,740; University of Pennsylvania Hospital, 11,521). The ages of nineteen of the asphyxiated children at the time of the follow-up examination varied from 2 years and 5 months, to 11 years and 8 months. A parent or sibling of each asphyxiated child was examined to form the control group. The author shows that a statistically significant difference in mental status exists between a group of children severely asphyxiated and apneic at birth and a control group consisting of their siblings or parents.

JAMES P. MARR.

Pregnancy. Complications

Perez, M. L.: The Etiology and Pathology of Some Spontaneous Ruptures of the Uterus in Pregnancy, *Obst. y ginec. Latino-Am.* 1: 509-524, 1943.

The author is not concerned with rupture of the uterus due to such conditions as congenital anomalies or surgical trauma due to cesarean section or myomectomy. He deals, however, with ruptures due to the eroding action of villi in cases of placenta accreta or hydatid mole and also with ruptures which result from degeneration of the uterine muscle, phlebectasis and adenomyosis. He also takes up ruptures due to scars from previous myometrial injury which took place during normal or abnormal labor. In the latter group, the author includes scars which resulted from uterine apoplexy, curettage and manual removal of the placenta.

J. P. GREENHILL.

Infantozzi, J., Ximeno, M. R., Crottogini, J. J., Granipietro, G., and de Santiago, A. P.: Pregnancy Near Term in a Uterine Horn and Tubal Gestation Near Term With Dead Fetus, *Obst. y Ginec. Latino-Am.* 1: 525-550, 1943.

The authors report a case of near-term pregnancy in a rudimentary horn of the uterus and an advanced tubal gestation which reached the eighth month. In studying these cases the authors discovered a new radiologic sign which permits differentiation between an advanced tubal pregnancy and a gestation in a uterine horn. In cases of rudimentary horn pregnancy, the fetal membranes are thick, whereas in extrauterine pregnancies the membranes are thin. Likewise, hysterosalpingography offers a means of differentiating between these two types of pregnancy. In cases of rudimentary horn gestation, the customary triangular shape of the uterus is absent. The uterus is longer, thinner, and corresponds to a horn of a uterus duplex. In cases of tubal pregnancy, the uterus retains its triangular shape, although it is deformed by pressure of the adjacent fetal sac.

J. P. GREENHILL.

Evans, E. Graham: *Anemia in Pregnancy*, Illinois M. J. 84: 317, 1943.

The author gives a brief review of the literature and discusses the factors which contribute to anemia in pregnancy. He cites his observations of 117 cases and emphasizes the importance of early and repeated blood examination during pregnancy and the post-partum period.

He concludes that 87 per cent of his patients showed at some time a hemoglobin reading of less than 69 per cent (10 Gm.). The color index is usually low. He advocates the use of ferrous sulfate in 15 to 30 grain doses daily, until a normal level is attained.

FRED L. ADAIR.

Sabathie, L. G.: *Heart Disease and Pregnancy*, An. Catedra de clin. ginec. 2: 289-297, 1943.

There are four important causes of heart disease in pregnant women: rheumatic fever, hypertension, syphilis and arteriosclerosis. Rheumatic fever is the preponderant etiologic factor, and about 90 per cent of pregnant women have this type of cardiopathy. Among the rheumatic heart conditions, valvular lesions are most frequent (70 per cent), particularly mitral stenosis. It has been estimated that one in each 5,000 pregnancies is complicated by congenital heart disease. Generally speaking, these patients tolerate pregnancy very well, since most congenital conditions that permit survival to maturity do not compromise seriously the procreative capacity in a woman. Cardiovascular syphilis is extremely rare in pregnancy, but this would be expected, since only 25 per cent of such cases occur from 20 to 45 years, and of these 25 per cent, only 18 per cent occur in women. Bacterial endocarditis accounts for approximately 1 per cent of heart disease in pregnancy. It is frequently caused by abortion in cardiac patients.

In the diagnosis, evaluation of symptoms should be a matter for collaboration between the obstetrician and the cardiologist. A previous history of rheumatic fever is always significant. Dyspnea, tachycardia and edema are of relative value. Early diagnosis of cardiac insufficiency in pregnancy is extremely important in prognosis. Another factor of prognostic importance is the classification. Prognosis is favorable in Type I (American Heart Association), and IIa, reserved in type IIb and bad in type III. In addition, there are patients with questionable cardiac insufficiency, in whom the prognosis is good, and another group, constituting about a fourth of all patients with cardiac symptoms in pregnancy, who have functional disturbances. Serious mistakes may be made in regard to such patients, if they are not examined by an experienced cardiologist.

The uncertainty of the prognosis in many instances presents a serious ethical problem to the obstetrician, and the advice as to whether the pregnancy should be continued is always an individual problem, in which many factors, including social, economic, psychic and religious, must be considered and evaluated along with the physical state.

J. P. GREENHILL.

Sodeman, William A., and King, Edward L.: *The Heart in Pregnancy-Prognostic Aspects*, South. M. J. 37: 235, 1944.

Functional capacity of the heart rather than the anatomical defect is generally held to be of most importance in offering a prognosis to the pregnant patient with cardiac disease. The classification as outlined by the New York Heart Association has been widely accepted. The author believes that neither functional capacity nor anatomic defect alone is all important. In general, the functional capacity seems to be more important but the age of the patient, auricular fibrillation, cardiac enlargement, aortic stenosis, hypertension, active rheumatic fever, congenital anomalies,

previous failure, bacterial endocarditis, and general systemic disease may play a part in prognosis. Even when all factors are considered, the prediction of the course which the disease will take in pregnancy requires decisions in an ill-charted field of medicine.

The author discusses each of the anatomical cardiac defects in relation to functional capacity and quotes his own plus the experience of others in their management. That a wide divergence of opinion exists among the best authorities in the management of the pregnant cardiac is apparent.

WILLIAM BICKERS.

Puerperium

Pereira, Joao Mario da S.: Incidence of Puerperal Infection Among 1,000 Deliveries, *An. brasil. de ginec.* 7: 271-283, 1942.

The author reports the excellent results obtained after adoption of prophylactic methods at the Maternity Hospital "Arthur Bernardes" under the direction of Professor Clovis Correa da Costa. The factors operative in reducing the puerperal morbidity to a minimum are: frequent vaginal examinations are avoided; on admission, the patient undergoes a thorough vulvar "toilet"; the instruments are thoroughly sterilized; vaginal instillations of 2 per cent mercurochrome solution are made every four hours. In retention of cotyledons and large fragments of membranes, manual evacuation is done followed by washing of the uterine cavity with boiled water. Sulfonamide compounds and estrogens are used in cases of repeated handling and manipulations within the genital canal. In the author's opinion, this combined treatment constitutes the best means of combating puerperal endometritis. Sulfanilamide in powder form is applied to the uterine cavity in some cases of infection; in others Mouchotte's method of drainage is employed.

With these prophylactic measures, the puerperal morbidity among 1,000 deliveries was 4.2 per cent. There was no mortality.

J. P. GREENHILL.

Duek, H.: Disinfection of the Vulva as Prophylaxis Against Puerperal Infection, *An. brasil. de ginec.* 8: 268-277, 1943.

The author employed a number of substances to disinfect the vulva during labor and checked his results by cultures. He found that the best substance for this purpose was 2 per cent mercurochrome. He claims that by the use of vulvar antiseptics, the incidence of puerperal sepsis was reduced in his Rio de Janeiro Clinic from 6.6 per cent to 1 per cent. He also discusses and compares the statistics concerning puerperal sepsis published from other countries.

J. P. GREENHILL.

Venereal Diseases

Ahumada, J. C., Gandolfo Herrera, R., and Sammartino, R.: Lymphogranulomatosis (Paltauf-Sternberg) of the Hypogastric Glands, *Bol. soc. de obst. y. ginec. de Buenos Aires* 22: 355-361, 1943.

The authors report a case in a woman, aged 34, whose symptoms of pain and tumor developed after an appendectomy performed when she was four months pregnant. Following the appendectomy an incomplete abortion occurred, necessitating two curettements. At operation, a tumor was found in the right parametrial region, filling and distending the broad ligament. The growth was hard, lobulated,

of firm consistency, the size of a small lemon, and intimately adherent to the posterior surface of the broad ligament and the pelvic wall. The ureter also was involved in the growth. The histologic picture conformed to that of lymphogranulomatosis of Sternberg in the third period of its development. It was impossible to follow the patient after she left the hospital.

The authors have found 12 cases of pelvic lymphogranulomatosis, including the one they report, with seven localized in the broad ligament. The first was reported by Luce in 1910, in a woman, aged 27, who presented a tumor similar to that described here; the patient died a month and a half after operation. Schlagenhauser (1911) reported the observation in a woman, aged 68, whose autopsy also showed tumor nodules in both parametria, with metastases in the bladder and ureter. Szenes, in 1928 reported a woman, aged 35, who at laparotomy was found to have intraligamentary tumor nodules on the right side. Autopsy two months later showed lymphogranulomatous formations disseminated in the right parametrium, uterus, both adnexa and bladder. The fourth case was reported by Levinski in 1930: a married woman, aged 37, was treated with deep radiotherapy. At autopsy, lymphogranulomatous formations were found in both parametria, uterus, adnexa, bladder and rectum. In the same year, Esau reported the case of a married woman, aged 52, showing at laparotomy an intraligamentary mass on the right side, which was removed easily. She died ten months later with no sign of local recurrence. The sixth case, reported by Burger, was in a woman, aged 42, with a right intraligamentary tumor which was removed without difficulty. The case reported here is the seventh of this type in the literature.

J. P. GREENHILL.

Osmond, T. E.: *The Modern Treatment of Gonorrhea in the Female*, Brit. M. J. 4331: 51, 1944.

The technique of examination and search for gonococci is described. Four grams of sulfathiazole are given every day for 5 days with a cure in the great majority of cases. If a second course of treatment is necessary, an interval of 5 days should elapse and the type of sulfa drug changed to the diazine or pyridine form. Symptomatic general treatment should also be given. Local treatment is of definite value in chronic cases, but in acute uncomplicated cases this is rarely indicated except for personal hygiene. Abscesses such as Bartholin's abscess should be drained. Various other complications are described and treatment mentioned.

To determine a cure one or two tests should be carried out at four-day intervals following completion of treatment, and then monthly examinations for at least three, and preferably six months before the patient is discharged as cured. These latter examinations should be carried out immediately after a menstrual period since it is at that time that gonococci, if present, are most easily detected. During pregnancy the same treatment should be carried out, care being exercised in the use of local therapy. Sulfa drugs are not contraindicated.

With regards to gonorrheal vulvovaginitis in children, the author advises strict isolation. Chemotherapy is the treatment of choice. Local therapy and the use of hormones are mentioned.

WILLIAM BERMAN.

Society Transactions

THE NEW YORK OBSTETRICAL SOCIETY

MEETING OF MAY 9, 1944

The following papers were presented:

Carcinoma of the Ovary Treated Preoperatively With Deep X-ray Therapy—Report of 3 Cases. Thomas J. Parks, M.D. (by invitation). (Will appear in a later issue.)

Ovarian Fibroma and Thecoma in Relation to Ascites and Hydrothorax (Meigs' Syndrome). Analysis of 78 Cases Including Some Experimental Data. I. C. Rubin, M.D., J. Novak, M.D., and J. J. Squire, M.D. (For original article, see page 601.)

Items

American Board of Obstetrics and Gynecology

Examinations

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Saturday, February 3, 1945, at 2:00 P.M. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year. All applications must be in the office of the Secretary by November 15, 1944.

All candidates are now required to be out of medical school not less than eight years, and in that time they must have completed an approved one-year internship and at least three years of approved special formal training, or its equivalent, in the seven years following the intern year. This Board's requirements for internships and special training are similar to those of the American Medical Association since the Board and the A. M. A. are at present cooperating in a survey of acceptable institutions.

A number of changes in Board regulations and requirements were put into effect at the Board's last annual meeting, held in June, 1944. These were designed to aid civilians as well as candidates in the Service. Among these is the waiver, temporarily of the A. M. A. requirement for men in the Army or Navy, especially for those who proceeded directly or almost so from hospital services into Army or Navy Service, upon a statement of intention to join promptly upon return to civilian practice. At this meeting the Board decided also to accept a period of nine months as an academic year in satisfying our requirement for certain years of training. This is only for the duration, and even men who are not eligible for Military Service but who are, nevertheless, in hospitals where the accelerated program is in effect, have been allowed to submit to us this short-time period of training in lieu of our previous requirements.

Beginning with the next written examination, which is scheduled to be held February 3, 1945, this Board will limit the written examination to a maximum period of three hours and in submitting case records at this time, all obstetrical reports which do not include measurements either by calipers and, as indicated, by acceptable x-ray pelvimetry, will be considered incomplete.

All candidates are required to take the Part I examination, which consists of a written examination and the submission of twenty-five (25) case history abstracts, and the Part II examination which consists of an oral-clinical and pathology examination. The Part I examination will be arranged so that the candidate may take it at or near his place of residence, while the Part II examination will be held late in May, 1945, or early June, 1945, in that city nearest to the largest group of candidates. Time and place of this latter will be announced later.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

SEPTEMBER 18, 1944.

Directory of Medical Specialists

The biographic data of the first two editions of the Directory of Medical Specialists include only positions (internships, residencies, or assistantships) held during the course of training of men up to the time of their certification by the American Boards, and hospital and medical school staff positions then currently held.

It is desired to extend this data in the Third Edition to include all formal hospital and medical school appointments, with dates held, even though now resigned, as well as records of all Military Service including commissions and dates, either in World War I, peacetime in the Reserve Forces or in the present war.

Thus, a chronologically complete sketch of a Diplomate's entire career is to be included in this Third Edition of the Directory.

Membership or fellowship in national or sectional (not local) special societies, and national general societies with offices held, and dates, in any of these, should be reported.

Membership in recognized international medical societies may be included, but honorary or other membership in foreign medical societies should not be reported.

Reference to the Second Edition (1942) of the Directory may be made for lists of medical societies to be included in one's biographic sketch.

Families or secretaries of men absent in Military Service are asked to complete or correct previous listings, or new forms now being mailed to those eligible for inclusion in the Directory. Only those certified by an Official American Board can be included, and there is no charge for this listing.

The foregoing notice is published in response to many inquiries, to assist those certified by the American Board who are now engaged in correcting their previous listings, or preparing new sketches for the Third Edition of the Directory to be published early in 1945.

Communications should be addressed to the Directory of Medical Specialists, 919 North Michigan Avenue, Chicago 11, Illinois.

American Journal of Obstetrics and Gynecology

VOL. 48

DECEMBER, 1944

No. 6

American Gynecological Society

Sixty-Eighth Annual Meeting, June 19 to 21, 1944

PRESIDENTIAL ADDRESS*

Woman in This Changing World

GEO. W. KOSMAK, A.B., M.D., NEW YORK, N. Y.

IT IS appropriate and customary on this occasion for one who has been chosen as your President to acknowledge his appreciation of the honor conferred by his selection for this high office. Accordingly, in all humbleness, I am prepared to do so. For to have headed, by force of circumstances for a period of two years, one of the oldest organizations of specialists in that branch of medicine to the progress of which it has devoted itself, is a distinction which merits this personal expression of gratitude and appreciation.

Among the duties devolving upon your President is that of making the Annual Address. Although it is a pleasant duty, the choice of subject necessarily constitutes for him a problem and as one looks back through the Society's Volumes of Transactions for suggestions from his predecessors, it becomes evident that the assignment has not been a simple one, for many of the incumbents of this high office have ventured outside the clinical fields with which perhaps they were most familiar, and have discussed a variety of academic and historical subjects. It is a temptation for an older man, and most of our Presidents were no longer young when they occupied this position, to select a topic with a literary flavor, or with a hero in obstetrics or gynecology as their subject. For this gave opportunity for pleasant reading and I was tempted to do the

*Presented at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

same. However, I found that most of the great men of the past whose careers were identified with our speciality, had been resurrected for this purpose, so I had to look elsewhere. Whether I have made a suitable choice must be left to my audience. For I want to venture into another field, a field which should be viewed by all physicians, and especially our particular group, with interest, with sympathy, and with understanding, for its discussion bears directly on the problems within our own sphere, which should deal with the welfare of womankind in general. And so in entitling my address, "Woman in This Changing World," I feel that I may have opened up a subject for discussion so endless and so volatile, that any hoped-for solution of the problems associated with it probably is impossible, at least in this immediate day and age. For one cannot fail to acknowledge the new position, social, economic, and even physical, which woman has assumed in this last century, and particularly, in these recent years since the world has become involved in a global conflict. For war has expedited the evident changes in our accustomed lives, and in this connection there are many contributing factors which cannot be overlooked, even if they bear only indirectly on our topic.

War, in a sense, has always afforded a stimulus to social progress, as well as in the field of the arts and sciences, and upon medicine devolves both the need primarily to care for war's participants wounded in conflict, as well as those in civil life affected by its destructions. War speeds the more rapid development of new measures in medical as well as in other fields. On the one hand, science has been called upon to expand its efforts to devise more effective ways to maim and to kill and on the other, to reduce the toll of the necessary fatalities and to care for those injured both in mind and in body. The former efforts are coexistent with the period of the war, the latter must be carried over into the restoration of the peace. What a boon to humanity has been the impetus to combat infection and shock, for example, by means previously slow to be adopted—chemotherapy, transportable blood plasma, and other procedures, now generally accepted. But these will contribute only in a restricted sense to the problems in which we are interested as specialists in a limited medical field. For woman will continue to present her problems, her physiology and her biologic status have not and cannot well be altered. Yet in this particular war, we have subjected her to strains and stresses far beyond what were formerly regarded as her natural capacities. In consequence there have been subordinated, among other things, what we as gynecologists must continue to regard as her natural functions, among which motherhood remains the most important. For, trite as the remark may seem, without motherhood, the world, as we know it, would cease to exist. Woman today continues her striving to become, what she terms, emancipated—she wants to be on a level with man—politically, socially, even physiologically. Perhaps this leveling process will benefit mankind, a mere male would be ridiculed and cast out if he disputed the aspiration. But seemingly, in this movement, priority is

no longer given to motherhood, modernism denies that this is the sole purpose of the sex. Admitting certain favorable results that have come from all this striving, can we set aside the hitherto accepted distinction between the sexes which Nature has ordained? There can be no human hybrids as there are among animals and plants developed solely for strength or size or beauty, but not for reproduction of their kind. And so while we may accept and perhaps welcome the advances which women have attained for themselves, there must eventually develop a limitation to these ambitions if there is to remain a bisexual world. For who will deny that the latter is an essential factor in the life of the planet which provides us with a habitation? Perhaps the situation is different on Mars—I do not know. At least on this earth, we are men and women, distinct as Nature had intended.

Therefore, one might view with some doubt the validity of certain statements made by Captain Mildred McAfee, President of Wellesley and now the Commander of the Waves, in a recent address in which she called upon women college graduates to face responsibilities as “people” and not just as “women,” for people as such, she claimed, are more important than men and women. The interpretation of this claim probably will vary with the individual reader, but would it not be better if, in admitting that women must do their part in carrying the common load, as she likewise acknowledges, that they do so as “women” and not merely as “people”? I cannot be made to believe that this is a distinction without a difference.

Woman has climaxed her previous efforts in this World War II and, as one studies the statistics of woman's participation in the present conflict, one is amazed by its extent. For it is not only the home front which is involved, the battle areas themselves have called into action large numbers of women as nurses, social welfare and canteen workers, the Wacs, the Waves, and others, impressed to supplement man power and to relieve men for more important actual combatant duties. The activities of women in this war are manifold, they do almost everything except to serve the actual weapons of death and destruction. And from all accounts, they have made themselves so invaluable by their excellent services, that the commanders in the field are asking for reinforcement of their ranks. The appeal made through the press, the radio, and the lecture platform is directed to the patriotism of women, it presents the glamorous aspects of wartime service and its attractions are set forth in glowing colors. But one may have doubts of the value of taking women away indiscriminately from their previously accepted duties and responsibilities. Less glamorous perhaps is the endeavor to enlist women in industries involved in the war effort, industries which had never employed women and in occupations formerly closed to them. This concerns not only single but married women. The Bureau of the Census may be quoted as stating that in March, 1942, there were 7,600,000 persons in this nation's labor reserve who said they were available for

full-time employment, of which 7,000,000 were women, most of whom were engaged in "Housework." In November of that year, the reserve had been reduced to 5,000,000, of which four and a half million were women, most of them married. These figures indicate that approximately 2,500,000 women were employed in war industries or other related activities during the intervening eight months. Today, their numbers undoubtedly are greater. These additions to available labor supply necessitated the introduction of many measures for health conservation, particularly in factories. A large proportion of these recruits to industry were in the 18- to 44-year group, namely in the childbearing age. As Dr. Charlotte Silberman of the Federal Children's Bureau stated in a recent admirable study of the subject, "it is difficult to obtain reliable figures of the incidence of pregnancy among women factory workers. Where satisfactory records were available, it was found that there were from 3 to 6 cases per 1,000 women per month." It should be noted, moreover, that more than 50 per cent of women workers were married, and this percentage will increase as the labor market narrows. It is unlikely however, that the reporting of pregnancy is accurate, there are so many more things to occupy factory managers. Nevertheless, maternity policies have had to be developed in industry, including the granting of leaves during pregnancy and for the necessary aftercare, all of which must exert a disturbing effect on labor turnover.

And in this connection, we must consider not only pregnancy in the increasing employment of women in industry but a multitude of other factors. The physical strains imposed on women workers have necessitated more stringent rules and regulations in their employment as regards absenteeism during certain periods, protection against hazards, hours for rest, as well as provisions for the care of the household and for unattended children left at home. This has constituted in many instances, a serious community problem, and brings us up sharply in evaluating woman's status as between being a war worker and a homemaker. Thoughtful women have voiced the dangers of these changed conditions in the home from a peace to a war footing. Providing shelter, clothing, food, family supervision, and elemental instruction, are responsibilities incumbent upon parenthood. But right now, the home is "short" on mother's time, and without it, the American home cannot function adequately. If these necessities cannot be supplied, the coming generation will be the sufferer. Already the growing incidence of juvenile delinquency has become a major problem. If we are to have a satisfactory postwar existence and an enduring peace, with the possible social upset brought about by woman's changing status, a beginning must be made now. The rush of women into war industry has deprived the home of maternal influences. The absence of mothers means the care of the younger children by outside agencies, and no care at all, in many cases, of the adolescent boys and girls. We are appalled by accounts in the newspapers of the rise of juvenile delinquency. But in

view of the lack of parental influences, we need not be surprised that great numbers of the rising generation have strayed from the paths of even ordinary decency and behavior, from mere mischief into actual crime. The police and social agencies are faced with a problem, the solution of which is a matter less for them than for the mothers of the nation. Homes disrupted by influences which should not have prevailed must be restored not from without but from within. The obligations of parenthood cannot be set aside. We are being deluded by the talk of population increase which is based on the bumper crop of babies reported in these recent years. After this, as after other wars, there will come a decline in births, and every child life saved today will have a substantial reflection on our future happiness and prosperity.

Let me quote in furtherance of the foregoing from a recent address by Margaret Craig of the School Health Bureau of the Metropolitan Life Insurance Company, who claims that the entrance of mothers into the war effort has had a deleterious effect on their children and, as she expressed it so well, a "rootless generation" is growing up, especially in the highly urbanized states. She said and very properly, "there seems to be a wholesale rejection of children in lieu of other interests based on the demands of living in a world at war. Where there should be more care and supervision, children are given too much responsibility for their years to carry." Citing the rise in juvenile delinquency, she asserted that "undemocratic habits of behavior are being established and children's sense of values are being thwarted because of the lack on the part of parents in establishing an environment where the real and fundamental things of life are given first place."

The figures previously presented of the number of women who have left occupations associated with activities long accepted as their province, afford an idea of the problems which must be faced in the near future. Their sudden adaptation to modes of life previously foreign to them must have had a psychologic as well as a physical effect. In a sense, they have been soldiers, or they have been made to believe that they are such. The transition from a peaceful existence into one with an entirely foreign environment, which subjects women to strains and stresses often different from previous experiences, may in many instances have been necessary and essential but, eventually there must come a time for readjustment, and we may need to formulate rehabilitation methods for women who have temporarily been absorbed by war industries just as we are doing for the returning soldiers. It will not be a simple matter although fortunately, women are more adaptable than men.

Another particular problem associated with the war, which is causing some concern, deals with the behavior of women to invalided soldiers returning to their homes. A man blinded or without a limb, discharged from a hospital with wounds healed but with a shattered mind, shell shocked, or racked with the aftereffects of tropical fevers—how

shall he be cared for, how helped to overcome the depression due to his war experiences? Psychiatric welfare workers, had we enough of them, might solve a part of the problem, but it is the wife, mother, sister, upon whom the greater portion of the burden must fall. For this she must be prepared, and it is to be hoped that her own previous separation from the home while engaged in a war service may not have taken from her that sense of responsibility and that helpful sympathy which is so essential to the successful carrying out of these important functions. And therefore, the rehabilitation of women war workers likewise in this sense is a matter for serious consideration. Who is to do it? I am not prepared to make a satisfactory answer, but I feel that it would be well if some of the propaganda efforts exerted on women through the press, radio, and other sources, as an appeal to their patriotism or the more lurid appeal to their pocketbooks, could likewise be developed in other directions.

The postwar adjustments in family life will involve great numbers of our people. Men and women in the Armed Forces, who may have participated in great historic events, living under conditions of exhilaration and excitement, or those who have labored under the attractions and distractions of other wartime employment, often with immediate high monetary returns, all will have difficulty in adjusting themselves to their former mode of life. There will be problems of the utmost complexity to be solved. For it has been said and very wisely, that "war not only destroys and damages property, it also destroys and damages people." We may include here the many war marriages often contracted on the impulse of the moment and subsequently subjected to periods of separation during which husband and wife undergo completely differing types of experience.

Having discussed certain prominent features dealing with the rapidly changing status of women in this more recent period of unrest in the world, it would appear of interest to review rather briefly the movement which has culminated in this striving for equality between the sexes. Far back in history woman was a slave and chattel, but this undesirable position no longer prevails except among those whom we may call the backward people of the world. After the Middle Ages, when Europe awakened during the Renaissance and later on when migration especially to the North American continent progressed, the property and social rights of women began to be recognized but aside from a few cursory efforts, her political and social status did not advance perceptibly until within the period of the last hundred years, and then mainly among the English-speaking nations.

This advance was designated as a movement of emancipation, emancipation in the sense of attaining equality with man, socially, politically, and economically, a really factual independence guaranteed in many instances by legal decree. The relationship of husband and wife no longer implied that the former was the master of the latter. Woman

attained a position where she no longer considered herself a mere bearer of children with its accompanying responsibilities. She entered, through her own and persistent efforts, the domain of the arts and professions and industry, previously largely sacred to man. She made a demand for greater respect and attention because of her attainments. But whether she will be able to combine all of these newer achievements with her primeval obligations, remains a problem for future adjustment. For speaking biologically, she must continue to exercise, willingly or unwillingly, the functions with which the Creator has endowed her. Calm and philosophical rather than wishful thinking is essential if we are to preserve a world in which the two sexes will reign not as competitors but as co-workers.

The position of woman, in a social sense and otherwise, has undergone great changes in this day and age. It is essentially a record of progress, but where and when will this progress be stabilized? I must admit my inability to make an adequate reply, nor can I with safety or assurance point to any prophet of either sex who would dare to do so. Will woman go on in her career to emulate man and then rest secure in the thought that she has attained this equality, or will she go on beyond this and occupy the stature of the famed Amazons of Greek legend and thus be the superior being physically as now perhaps she is intellectually? In this connection I would like to paraphrase the title of a widely read book written some years ago by Henryk Sienkiewicz, in which there is recounted an ancient legend of the early Christian era. Saint Peter, fleeing from Rome to escape crucifixion as a martyr, meets his Lord Christ on the Appian Way. "Domine, quo vadis?" he explains. "Lord, where goest thou?" "To Rome, to be crucified again," is the reply. And the Apostle turns back to his martyrdom. I do not deem it irreligious if I permit myself to exclaim in a similar fashion, acknowledging the change in time and circumstances—"Femina, quo vadis," "Woman, where goest thou?"

Woman's career in our country has been of signal interest onward from the Colonial Period, through the expanding migration to the unsettled West during the middle of the last century, through the era of the strife between the North and South, and through the later decades when political rights were conferred upon her, and she in considerable numbers, entered the ranks of the professions, business and industry. "The sweep of American culture has brought woman to a near equality with man in almost every aspect of her social career," states Prof. Groves in his book on *The American Woman*, and he regards it as one of the most characteristic and important results of the evolution of the American people. But, he adds very wisely, "although it brings a long continued effort near fulfillment, it is not a solution born of the difference between the man and the woman." To quote further, "although some of the problems may be labeled *finis*, others as perplexing, as compelling, as pressing, although on a higher plane, take their place.

There are three parties concerned as adjustments to the new order are attempted: woman, man, and biologic nature. The third has such commanding authority that if it decides against present trends, society, to survive, must find its way back, driven by pain-pressure to the more ancient ways of man-woman relationship. In the new order woman not only has a more active part, she has assumed a greater social responsibility and she has manifested the same self-determination that possesses man."

These well-expressed thoughts, however, should lead to a searching inquiry in another direction, namely, whether we can balance these social strivings and attainments with what Dr. Groves designates as "biologic nature." And here likewise, we must give attention to the acutely developed changes associated with our present world-shattering conflict.

Naturally, neither peoples nor governments can remain static forever—such changes as are concerned with material matters may be accomplished within comparatively short periods, as history has shown, but biologic changes are only brought about by the extremely slow process of organic evolution. The male and female sexes (all through Nature) have remained separate and distinct, it is only among certain of the lower forms of animal life that bisexual individuals exist, such as the lowly snail which, while it exercises certain instincts, still remains a snail, with limited ambitions to say the least. Men and women may develop equalities in a social sense, but biologically speaking, they must and can only exist as men and women. There is no place for a neuter gender as among the bees.

At a gathering such as this, devoted largely to a consideration of the progress in a recognized medical specialty, it is difficult nevertheless to divorce one's mind from the surrounding upheaval, for the world-shaking political events and social changes that accompany the struggle for a supremacy of arms, must have a bearing on our thoughts of what the future holds in store. If this means a change in our mode of life, man alone will not be concerned, woman must likewise take her part. The equal participation of both sexes in social, economic and other activities, has constituted the basis of a widely distributed propaganda in recent years, which insists that woman is to have equal privileges as a voter, as a wage earner, she is not to be discriminated against in any respect because of her sex. This attitude may be reasonable and justifiable, and in accord with modern thinking, but may it not deprive woman of some of that respect, devotion, and attention which she has always claimed and usually received without question? Probably a man will be designated as narrow and prejudiced, if he fails to agree completely with this tendency, especially when one cannot put aside the thought that the biologic status of woman in this world is incapable of alteration by a decree of law or by edict.

For it must not be forgotten that parenthood and the home are the essential factors in maintaining the world's population balance, its happiness and its prosperity. No matter how far-reaching the striving for independence by either sex and especially by women, that essential cannot be thrust aside. People may say, why this worry when we are having that bumper crop of babies in this country, to which reference already has been made. But when we realize what an inroad the war is making on marriage and home life, there must continue to be a preaching and a plea for the conservation of motherhood. It is estimated that almost three million babies were born in these United States during 1942, in 1943 there may be less. But the birth rate of 21 per thousand of population in 1942, is less than the 25 per thousand of the last war. One of the factors which has brought about the recent increase in births undoubtedly has been the greater number of early marriages due to the induction of our young men into the services. War brides mean war mothers, there may be thousands more of them if the draft continues, but the preparations for motherhood are not given thought in these hurried marriages, nor the responsibilities associated with parenthood. Although it is unfortunate that our young people give so little consideration to the consequences, nevertheless every effort must be made to secure for these prospective mothers the care which their condition demands. The government has taken note of this and has provided through the Emergency Maternity Act the necessary funds for the confinements of the wives of soldiers of the lower ranks. The extent of this activity must become evident from the fact that now over 300,000 women have applied for these services.

The mother is the fountainhead of a normal and successful family life. The latter has sustained some severe shocks in these war years. Not only have families been dispersed by the absence of fathers in the Armed Forces, but the widespread migrations to war production centers have done away with established customs and associations. Thus, families are broken up and have lost their significance in the social structure. Motherhood under these conditions becomes an even greater trial, and the dignity of parenthood has been sacrificed in many instances to expediency. The whole structure of our civilization may be undermined unless we give full recognition to the importance of the mother as the guiding influence in family life, and accord to her that attention which even the demands and exigencies of the war must not be permitted to destroy.

In this connection, it may be of interest to take note of the proposal that women be represented at the conferences to be held for the maintenance of the peace, after the present distraught world emerges from the conflict. It is claimed that there should be as many women as there are men, because women have qualified themselves as participants by their studies of the perplexing problems associated with the war. There are numerous questions to be decided for this postwar world for the

solution of which women perhaps are as well if not better qualified than men, and it is to be hoped that they will be considered by the sex to which they are so closely related. For this has not only been a struggle for power, it is a struggle for the preservation of free thought, of liberty, and of those conditions which will make the future world a pleasant and satisfactory place for mankind. And there is no better striving than that which will insure us that the family and motherhood are the essential factors in its preservation. I feel that here, medicine has a part to play, for it has had an active part in the conduct of the war and likewise it will have equal responsibilities in the peace which, let us hope, is not too far away. It has long been recognized that good health and the welfare of the State in both a social and a political sense are inseparably connected, although the efforts at a solution of the related problems are by no means fully developed or generally accepted.

The advances which have been recorded in preventive measures to check disease in these recent years, constitute an outstanding evidence of progress. This includes noteworthy changes in our own specialty which it is scarcely necessary to detail here. One need only refer among others to the improvements in operative technique, in the handling of malignancies, in substitutional hormone therapy, and above all, in the efforts to lower maternal and infant mortality and morbidity in childbirth. Particularly in the latter field we, as gynecologists and obstetricians, bring ourselves into close relations with the problems of population preservation and maintenance. This may appear an academic subject, yet it has important practical aspects for which physicians must assume a definite responsibility.

The growth and maintenance of population in the past has been largely influenced by natural and social factors, including environment, economic status, migration, etc. Artificial control of childbearing has, in more recent times, likewise received careful study and attention, to a greater extent perhaps by eugenists and sociologists than by the mass of the medical profession. To the latter has been assigned a subordinate task, namely, to carry out recommended procedures. The enthusiasms of the advocates for "birth control," have outweighed to some extent the more conservative attitude of those less inclined to interfere with Nature's dictates. However, there are arguments on both sides which must be carefully considered, without prejudice or hysteria, if we are to arrive at a sane and sensible evaluation of the matter. To begin with, it must be admitted that the medical profession as a whole, has been hesitant to lead or even to participate in any attempted solution of a problem which has been seized upon by groups of well-meaning but often overenthusiastic individuals, who believed that a reformation of our entire social structure would be accomplished by a widespread adoption of their program for the control of conception. Perhaps parenthood in the broader sense, has been governed in the past too largely by chance, and the thought of a controlled parenthood limited to those

who considered themselves more aware of its responsibilities. But it has also become recognized that childbearing has implications which apply not only to the individual but to the status of the race, the community, and the nation. These are factors which we are apt to forget in a wave of enthusiasm for a new and untried movement.

Normal and sustained growth whether in a race or in a tree, would appear essential to stability in many senses. Overpopulation in a country or overgrowth in a forest may perhaps be undesirable. Among the peoples of this earth, the unrestrained growth in numbers of the yellow and brown races in particular has led to the fear that they would in time displace the whites by overrunning the domain of the latter. However, in this connection, we must also admit that what we term a higher degree of civilization, has reduced natural fertility. Although it may take time, we may assume that unrestrained increases among those races which we look upon as inferior, will be subjected to similar influences. In the meanwhile, there is still plenty of room left on this earth to provide adequate living space and nourishment for the expansion of those who believe themselves crowded out. Therefore, the bearing of children and this at the most opportune period of life must be encouraged and not hampered. It cannot be put aside as a subsidiary function by either women or men, it must remain one of the most important and outstanding functions. It should be needless to further expand this point of view.

All of the foregoing should bring us back to our thesis, namely "The position of woman in this changing world." We must acknowledge the fact that it has changed, and we cannot deny that these changes have been radical and revolutionary. On the whole, they may be accepted as indicating progress, but how far this will go is a question for future generations to determine. It has become more than an academic problem.

I trust that what I have said will not be interpreted as in any way belittling woman's efforts to place herself on an equal footing with the opposite sex. Her striving is admirable and not to be criticized, if it can be directed along lines which will not take away from her the high esteem in which she is now held as a woman. She is the equal of man in many ways, but it would prove a dull, drab, and weary world if she no longer maintained that position of love and respect and admiration which is her due. Let us hope that some of the sudden transition brought about by the war may not be a permanent one, in so far as it concerns woman's entry into those fields of activity which are foreign to her natural capacities. For, superior to all other and immediate considerations, women must continue as the mothers of the nation, this is their outstanding function and responsibility.

THE RELATIONSHIP OF GRANULOSA-CELL TUMORS OF THE OVARY TO ENDOMETRIAL CARCINOMA*

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GRANULOSA and theca-cell tumors may be associated with such excessive and abnormal endometrial hyperplasia that a histologic pattern indistinguishable from adenocarcinoma results. Case reports have been published by Dockerty¹, Porter and Bramhall,² Stohr,³ Russell,⁴ and Schroeder.⁵ Dockerty found 3 carcinomas of the endometrium in 32 cases of granulosa-cell tumor, and 1 carcinoma of the endometrium in 10 cases of theca-cell tumor and concluded, in part, that "this incidence of 10 per cent seems more than coincidental and raises the question of the carcinogenic properties of estrin."

Three additional cases are included in the following report and serve as a basis for comparison of theca- and granulosa-cell tumor-induced hyperplasia and true carcinoma of the corpus uteri.

Apart from the effects of granulosa-cell tumors on the endometrium, the whole question of the relationship of the ovary to corpus cancer remains unanswered.

Many authors have presented evidence in support of the opinion that estrogenic hormonal stimulation is a major factor in the causation of carcinoma of the uterus. Herrell⁶ stated that in his experience, carcinoma of the body of the uterus had not been observed in the absence of the ovaries.

Ovarian follicular activity probably continues for variable lengths of time in nonovulating, involutional ovaries, and is perhaps responsible for post menopausal endometrial hyperplasia as described by Novak and Yui.⁹ But whether or not it may account for the development of corpus cancer is an open question. Reports of authentic instances of carcinoma of the body of the uterus in surgically castrated women would have an important bearing on this question. In a personal communication Dr. F. A. Pemberton states that G. Van S. Smith has reported 3 cases occurring 15 years after bilateral oophorectomy.

Cases of corpus carcinoma in women previously rendered "menopausal" by irradiation have been recorded by Scheffey,⁷ but it is evident from the report by Smith⁸ that recrudescence of ovarian function may occur after heavy irradiation. Therefore, roentgen ray or radium "castration" cannot be taken as an absolute equivalent of surgical castration.

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Jones and Brewer¹⁰ studied the ovaries and endometriums of 68 premenopausal patients with endometrial carcinoma and concluded that the ovaries may function normally, and the uninvolved portion of the endometrium may be normal and respond normally to ovarian stimulation. They believe that the etiologic significance of hyperestrogenism, or the unopposed action of estrin in endometrial carcinoma is not shown in their series of cases.

In further investigation of this question, we have studied a series of six hysterectomy specimens, including the ovaries, in corpus carcinoma, in order to determine whether or not hyperplasia of ovarian stroma, interstitial cells or follicular lining cells were associated with carcinoma. This study showed no constant relationship, and it was found that the ovaries were either partially or completely atrophic in all instances. The amount of deeply basophilic mesodermal tissue present in the ovarian stroma, and not demonstrably connected with follicular structures, was variable and while present in considerable amounts in some cases, was almost entirely absent in others. A further series of 15 corpus cancers was studied for histologic comparison with endometrial hyperplasia associated with granulosa-cell tumors.

Examination of such specimens provided an opportunity for comparison of the growth characteristics of corpus carcinoma and the condition of excessive proliferation caused by granulosa-cell tumor.

The most important features of corpus carcinoma are its progressive growth with continuous and irreversible proliferation, with invasion of the myometrium and establishment of metastases. Some of these features are lacking in many true carcinomas and in all reported cases of excessive hyperplasia, including our own.

Case Reports

CASE 1.—Patient, aged 60, para V, menstruation normal with menopause at 45 years. Started bleeding at 52 years of age. Two years later, her physician found a uterus "twice the normal size" and diagnosed myoma uteri. Two years later, she was examined, bleeding had continued, was more severe and quite constant. The uterus was slightly larger and a cystic tumor was felt on the right side posterior to the uterus. Operation was refused.

Not seen until two years later, in May, 1943. Bleeding had continued, was at times profuse, quite constant, often watery, without odor.

The patient had the appearance of malignancy. The hemoglobin was 45 (Sahli). The uterus was symmetrical, three fingerbreadths above the symphysis. The cervix was hard, patulous and exuded friable material. The cystic tumor was approximately two inches in diameter.

A total hysterectomy with bilateral salpingo-oophorectomy was done. At the time of operation, there was some leakage of carcinomatous material from the cervix.

In July, 1943, the patient returned with recurrence in the vaginal vault. X-ray treatment was instituted with improvement, but in September, she returned with symptoms of a partial intestinal obstruction.

tion. A laparotomy was performed, there were no nodules from which a biopsy could be obtained. The pelvis was filled with densely adherent loops of intestine and fibrous fixation of the pelvic tissue. Ascites was present. Nothing could be done to improve the condition which was undoubtedly the result of intensive x-ray treatment. A few days following operation, a fistula occurred between the intestine and vaginal vault which relieved the obstruction. She died in January, 1944, in a small Colorado hospital. No autopsy was obtained.



Fig. 1.—Uterus with endometrial and endocervical overgrowth, and granulosa-cell tumor of the ovary.

Gross Description: M. P. 5003. The specimen consists of the uterus, tubes, and ovaries. The uterus measures 11.5 by 8 by 7.5 centimeters. It is enlarged, globular, smooth externally. The myometrium is 2.5 cm. thick, and is pale, uniform without a sharply defined endometrial border. The endometrium is from 0.5 to 2 cm. thick and extends in bays 0.5 to 1 cm. deep into the myometrial wall. It is light gray, polypoid, with several large masses extending downward partially through the endocervical canal. The cervix is large, with thick ragged endocervical lining. The left tube measures 5.5 by 0.4 to 1 cm., being larger, with less evident atrophy than is usually the case after the menopause. The left ovary measures 2.5 by 2 by 0.5 centimeters. It appears to be completely atrophic. The right tube measures 5 by 0.4 to 1 cm. and is similar to the left. The right ovary is incorporated in a partially cystic tumor measuring 7 cm. in diameter. The serous surface is smooth. The cystic portion is composed of the tunica albuginea, forming the wall, and the lining is smooth. The content is serous fluid. The remainder of the ovary is solid with whitish tumor tissue, showing a faint yellowish tinge in some areas, arranged in a coarsely lobular mass measuring 3.5 by 2.5 by 2.5 centimeters. (Fig. 1.)

Microscopic Examination: The ovarian tumor is composed of fibrous stroma infiltrated by cords of basophilic cells, polymorphous, and variable in size and arrangement. A follicular arrangement is found in some fields (Fig. 2), while in others, there are more solid zones made up of closely grouped cords, often with clefts between them. In still others,



Fig. 2.—Granulosa-cell tumor of the ovary ($\times 170$).

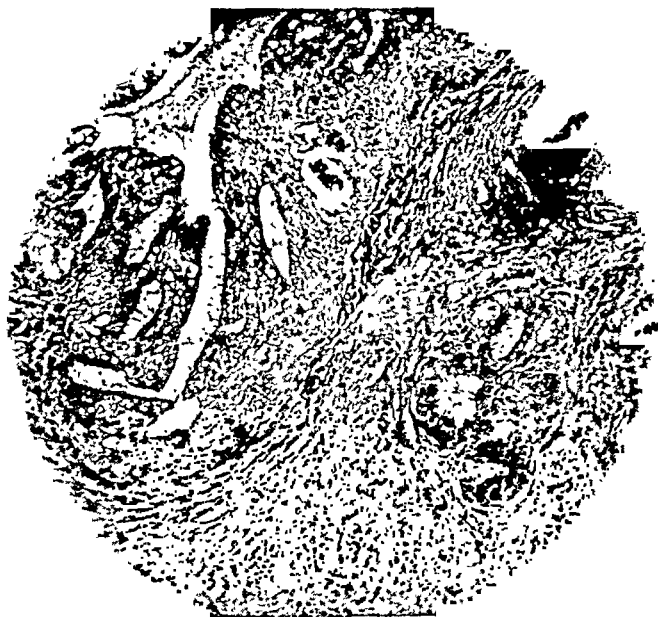


Fig. 3.—Section of cervix, showing hyperplasia and metaplasia of the endocervix ($\times 100$).

the cords extend into the stroma in single units, and in parts a tendency to radial or rosette grouping, with centrally placed Call-Exner bodies is found. Mitotic nuclei are present but not numerous. No evidence of extension through the tunica albuginea or invasion of the mesovarium can be found.

Sections of the corpus uteri and cervix show profound hyperplasia of endometrium and endocervix. In the cervix, the entire canal from the external os upward is lined by irregularly stratified and papillary epithelium, partly squamous and partly mucoid (Fig. 3). There is no tendency toward invasion of the stroma of the cervix.

In the uterus the epithelium is columnar, with abundant mucoid secretion. The arrangement is glandular with papillary excrescences. (Fig. 4.) The cells are uniform in size, with basal nuclei and pale, neutrophilic cytoplasm. Nuclei in mitosis are fairly numerous. The myometrial fibers are large and the uterine wall is thick. The glands are present between muscle bundles, chiefly in the superficial zone. The outer two-thirds of the myometrium also are invaded.

Where endometrial tissue is present within the myometrium, only glandular elements are represented, and endometrial stroma is lacking, which tends to eliminate endometriosis as an explanation of this finding.

The pathologic diagnosis was granulosa-cell tumor folliculoid type, of the right ovary, and adenocarcinoma, corpus uteri.

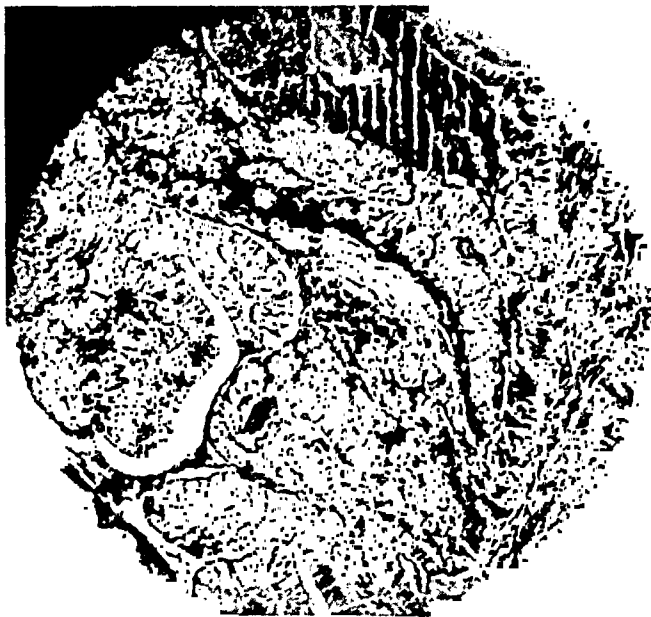


Fig. 4.—Section of uterus showing papillary adenocarcinoma of the endometrium ($\times 100$).

CASE 2.—A. 2714. The patient was a 79-year-old white widow, who had complained of vaginal bleeding for the past 10 years. There was no definite time interval between bleeding spells. She stated that a physician had told her 5 years previously that she had a tumor, but that nothing should be done. Three days before entry, the patient had a severe hemorrhage which stopped with bed rest. On the day of entry another profuse hemorrhage occurred.

Physical examination disclosed a well-developed, well-nourished elderly white woman. The breasts were large, firm, without masses or tenderness. There was a firm movable mass filling the lower abdomen and pelvis. It was irregular, soft, and rose to 4 fingerbreadths below the umbilicus. The vulva was firm, not atrophic. The blood pressure was 180/95.

Laparotomy was performed, disclosing a large ovarian tumor, in part retroperitoneal, strongly adherent to the sigmoid and small in-

testines. The uterus was enlarged and was removed with the ovarian tumor. The immediate postoperative condition was fairly good, but on the following day, the patient became comatose with rapid, shallow respirations. She died 48 hours after operation. Autopsy was performed 3 hours post mortem.



Fig. 5.—Cut surfaces of granulosa-cell tumor of the ovary and attached portion of uterus showing polypoid overgrowth.

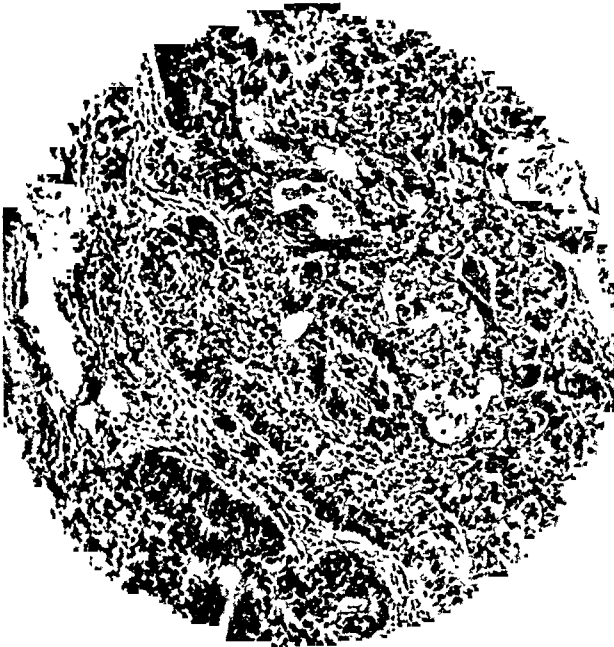


Fig. 6.—Section of uterus showing endometrial adenocarcinoma ($\times 100$).

The surgical specimen consisted of the uterus, both Fallopian tubes, and tumor of the left ovary (Fig. 5). The uterus measured 8 by 8 by 6.5 cm.; the serosa was intact. The myometrium was 1.7 cm. thick, yel-

lowish, and rubbery. The endometrium was unevenly thickened, polypoid, friable, and yellowish. Gross evidence of myometrial invasion was lacking. The right Fallopian tube merged with the ovarian tumor, which was 15 by 11 by 6.5 cm. in size, smooth externally, with shaggy gray-red bands where adhesions had been separated. Cut surfaces of the tumor were partially cystic, with abundant soft faintly yellow lobulated tissue surrounding the cysts. There was one large cyst 5 cm. in diameter which contained a single polypoid tissue mass and was filled with cloudy yellow fluid.

Microscopically, the myometrium was normal, without marked atrophy. The myometrial—endometrial border was uneven, with zones in which both stromal and myometrial invasion by endometrial glands was demonstrable. The endometrium was composed of closely grouped tubular glands with tall columnar epithelium of decidedly atypical appearance (Fig. 6). The gland lumina contained mucin and cellular debris. The epithelial cells were frequently hyperchromatic with

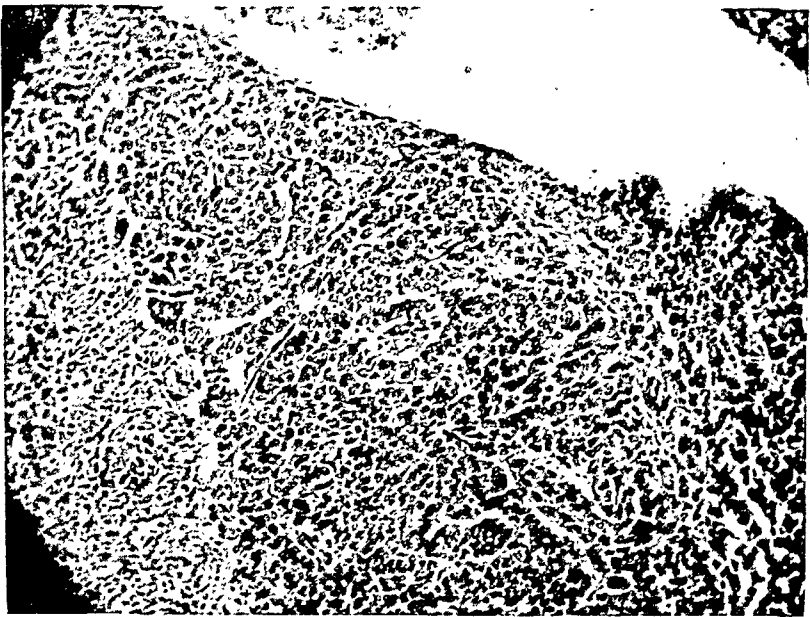


Fig. 7.—Granulosa-cell tumor of the ovary ($\times 170$).

numerous mitotic figures. Islands of squamous cell metaplasia in the glandular structures were present. The large polypoid masses of endometrium were in no way different from the endometrium lining the uterine cavity in general. The hyperplasia was equally great in the fundus and the lower uterine segment, which included the upper portion of the cervix, but did not extend to the external os, which was obtained in the autopsy specimen, and showed normal stratified squamous vaginal mucosa, with several old Nabothian cysts. Above the external os, the endocervix contained normal but autolyzed tubular glands for a short distance, 0.8 cm., and above this point the epithelium was glandular and hyperplastic.

The right Fallopian tube was entirely normal, with no evidence of senile atrophy. The right ovary showed complete senile atrophy.

The ovarian tumor was composed partly of small, dark basophilic cells in coarse lobular grouping, often arranged in trabeculae or rosettes about a hyaline acidophilic central mass. The cysts were lined by multiple layers of these cells, and masses of them nearly filled some cyst

cavities. The remainder of the tumor was made up of small fusiform cells lacking any trabecular arrangement, but tending occasionally to form imperfect rosettes, lying in a fibrous stroma, with marked edema in some zones. (Fig. 7.)

The mammary gland tissue, obtained at autopsy, showed dense fibrous stroma supporting numerous ducts lined by double layers of cuboidal or columnar epithelium. Many ducts were dilated, and practically all contained a granular mucoid precipitate (Fig. 8). Glandular spaces lined by large eosinophilic epithelial cells were numerous. In these the epithelium was hyperplastic and formed papillary, ingrowths nearly filling the lumina. The pathologic diagnosis was granulosa-cell tumor, trabecular type, of the left ovary; adenocarcinoma, corpus uteri; and hyperplasia of the mammary glands.

The specimen of the following case was presented to the Department of Pathology of the University of Colorado, by L. E. Likes, M.D., of Lamar, Colo.:



Fig. 8.—Section of mammary gland showing duct epithelial hyperplasia ($\times 100$).

CASE 3.—M. P. 5062, white woman, aged 62, menstrual history unimportant, menopause at 45 years. The present history dates back three years, when spotting occurred to appear again one year later. Eleven months later bleeding occurred with small amounts up to the time of operation.

Pelvic examination revealed the cervix smooth, healthy and very firm. The uterus was about the size of a two-month pregnancy. Treatment consisted of radium application followed by hysterectomy.

The pathologic specimen consisted of the uterus with both ovaries and the right Fallopian tube. It had been fixed in formaldehyde solution. The uterine cavity had been partially opened and a mass of endometrium protruded through the opening. The uterus was globular and approximately 6 cm. in diameter. Cut surfaces showed a solid endometrial mass filling the uterine cavity, and apparently invading the myometrium to a depth of 1 cm. in several areas. The left ovary measured 2.7 by 1.7 by 0.9 cm. in size and appeared completely atrophic.

The Fallopian tube was not remarkable. The right ovary was enlarged, measured about 3 cm. in diameter, and contained a lobular, yellowish, solid tumor. (Fig. 9.)

Microscopically, the right ovary is found to contain an encapsulated tumor composed of spindle cells of fairly uniform size with fibrous strands of varying density and numerous small blood vessels (Fig. 10).

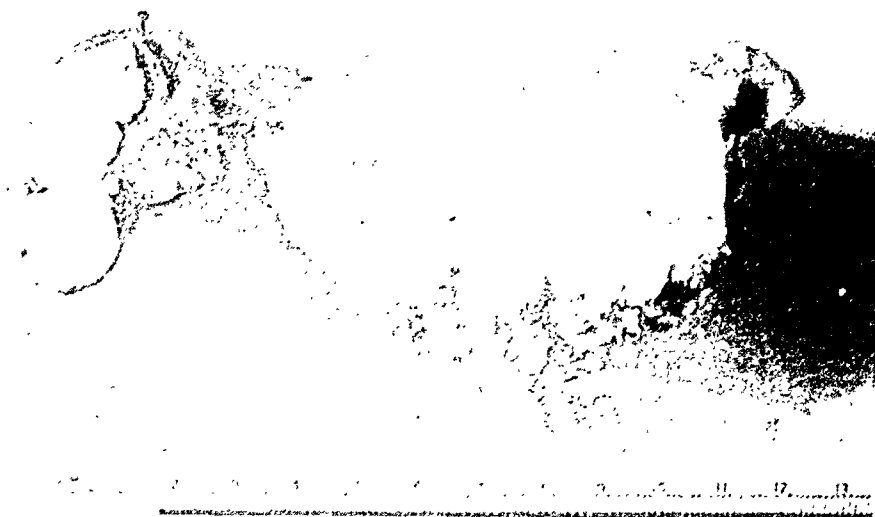


Fig. 9.—Portion of uterus showing endometrial overgrowth and attached theca-cell tumor of the ovary.



Fig. 10.—Theca-cell tumor of the ovary ($\times 170$).

Frozen sections stained with sudan III showed the presence of many small globules of fat or lipoid in the cytoplasm of the spindle cells and free in the interstices. No follicular structures or cysts were present.

Sections of the uterus showed a complete conversion of the endometrium into a papillary and glandular mass of atypical columnar epithelium supported by delicate connective tissue cords. The nuclei

were basal, with frequent mitotic figures. The cytoplasmic staining was variable, with groups of clear cells. Mucin production was scanty in some areas, abundant in others. The myometrium was invaded by groups of epithelial cells in glandular formations (Fig. 11). The pathologic diagnosis was adenocarcinoma of the endometrium with invasion of the myometrium and theca-cell tumor of the right ovary.



Fig. 11.—Section of uterus showing adenocarcinoma of the endometrium with myometrial invasion ($\times 100$).

Discussion

In each of these cases the histologic appearance of the endometrium is sufficiently hyperplastic and atypical to be classed as adenocarcinoma.

A search for definitions as to what constitutes carcinoma of the body of the uterus yields only equivocal criteria. Both Ewing¹¹ and Novak¹² follow the precepts of Ruge and Veit in dividing corpus carcinomas into circumscribed and diffuse growths. Ewing states that the cervical canal is rarely involved in corpus carcinoma, and that the integrity of the myometrium is the chief factor in the favorable prognosis of many uterine cancers. Also, according to Ewing, the muscular wall may become thin while still free from invasion.

Proof of malignancy would be furnished by perforation of the thinned-out wall with peritoneal extension; true infiltration of the myometrium by tumor cells; lymphatic or blood vascular extension and metastasis.

In Novak's opinion, although invasiveness is looked upon as the most decisive feature of cancer, the absence of stromal invasion by the epithelium should not influence the diagnosis when other characteristic features are present.

Thus, there can be no strict limitation of the definition of corpus carcinoma from the histologic point of view unless some or all of the

above-mentioned features are insisted upon, and these are to be expected only in late cases.

Practically, accurate diagnosis of corpus carcinoma is made from curettage specimens in which myometrium is lacking. In such cases invasiveness can only be estimated, and the extent of the growth cannot be determined.

Endometrial hyperplasia which duplicates the histologic features of adenocarcinoma of the uterine body may accompany granulosa-cell tumors of the ovary. In our Case 1, the endocervix also is hyperplastic. There is no histologic criterion which enables us to distinguish this condition from adenocarcinoma, yet in one of Stohr's cases, that of a woman before the menopause, a normal menstrual cycle was resumed 6 weeks following the removal of the granulosa-cell tumor. Curettage after 8 weeks showed a typical early secretory phase of the endometrium, and the patient remained well with a normal menstrual history for five years.

This case of Stohr's is remarkable in that only the ovarian tumor was removed. The estrogenic influence of the remaining ovary was not abolished and yet the endometrial hyperplasia regressed. This case provides evidence of the direct relationship between the ovarian tumor and the endometrial hyperplasia, considered by Stohr as adenocarcinoma, and in addition, indicates that such proliferation is reversible.

It remains a question as to whether or not a true carcinoma of the endometrium would regress if all abnormal sources of estrogenic hormones could be removed.

According to Taylor, three sources of an excessive supply or abnormal type of estrogenic hormone in the human may be considered: from follicles, as in follicular (functional) cysts; from ovarian tumors, as in granulosa-cell and theca-cell tumors; and from an extraovarian source.

In the third instance, the presence of estrogenic substances in male urine and in the urine of females after the menopause and after castration may be cited.

As has been suggested, extraovarian estrogenic substances may be formed in both sexes in the metabolism of cholesterol and bile acids, and chemically related carcinogenic substances may likewise originate in the same manner.

From the report of Jones and Brewer,¹⁰ it appears that normally functioning ovaries do not prevent the development of endometrial carcinoma, and that hyperestrinism or the unopposed action of estrin is not responsible for such development. It is possible that all endometrial carcinomas do not have the same cause or causes.

A further search for etiologic factors within the ovary may still be indicated, however, because of (1) the apparent infrequency of endometrial carcinoma in surgical castrates, (2) the frequency with which

endometrial carcinoma and granulosa- and theca-cell ovarian tumors are associated, and (3) the spontaneous regression of an "adenoma malignum" type of endometrial hyperplasia following removal of a granulosa-cell tumor of the ovary, in Stohr's Case 2.

Conclusion

Two additional cases of granulosa-cell tumor and one of theca-cell tumor of the ovary associated with adenocarcinoma of the corpus uteri are reported. The role of the ovaries in carcinoma of the uterus is discussed. The question of definition of cancer of the corpus uteri is reviewed.

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Discussion

DR. JEAN PAUL PRATT, Detroit, Mich.—Having had the opportunity of reviewing the prepared sections that Dr. Ingraham kindly sent me, I find the diagnosis of adenocarcinoma of the uterus and hyperplasia of the endometrium can readily be accepted. Furthermore, the diagnosis of granulosa-cell tumors of the ovaries is obvious from the appearance of the sections. The clinical history is typical of adenocarcinoma of the uterus for, in each case, the uterus was enlarged and bleeding appeared in women well past the menopause.

To present 3 cases in which adenocarcinoma of the uterus is associated with granulosa-cell tumor of the ovary is an unique experience. I have just reviewed 135 cases of adenocarcinoma of the uterus, and none of them were associated with functioning tumors of the ovary. On the other hand, 5 cases of granulosa-cell tumor of the ovary were not associated with adenocarcinoma of the uterus.

Presentation of the three cases naturally raises the question of carcinogenesis. Since Leo Loeb, 25 years ago, predicated a hormonal etiology of cancer of the mammary gland, a vast array of evidence regarding his theory has been presented. Investigations were soon extended to other organs including the uterus, but the results have been less conspicuous. Among the early investigators in this field, Edgar Allen employed large doses of estrogens administered to monkeys over a long period of time. Considerable hypertrophy of the cervix resulted, but even with the addition of trauma no cancer developed. Other experimenters have been no more successful in producing cancer of the cervix. Experimental study of cancer of the uterus has been limited because no species of animal has been found which possesses a strong hereditary susceptibility to cancer of the uterus.

Inferences from animal experiments are valuable indicators for procedure in clinical investigation. The extreme variations of susceptibility to cancer in different species and strains emphasize the importance of heredity. The relative speed with which experiments in heredity in animals can be concluded tends to discourage similar studies in man whose life span by comparison is so much longer. A sufficient number of family histories has been recorded to show that certain types of cancer are strongly hereditary while other types show no hereditary tendencies. Of particular significance in this connection is the record of twins. In 50 per cent of those who had cancer, the other twin developed cancer at the same site and at approximately the same age. Could Dr. Ingraham give us any further family history in his cases?

The majority of cancers of the uterus occur after the menopause. If one assumes hormonal influence as important in the incidence of cancer of the uterus, would he not expect the growth to appear before the menopause?

The extensive use of estrogens affords another opportunity for clinical investigation of carcinogenesis. There are now many cases on record and many more not recorded in which enormous doses of estrogens have been given over a long period of time, but no carcinomas developed. Adding the greater incidence of cancer after the menopause to the extensive use of estrogens without inducing cancer speaks against the ovarian hormones as carcinogenetic agents in cancer of the uterus.

Is the growth of cancer due to inciting certain cells to growth or to release of inhibitors in the environment, or both? The cause of cancer remains a very complex problem. The final solution rests with further clinical observations and interpretations. Dr. Ingraham's contribution invites further observation on the uterine ovarian relationship.

DR. GRETE STOHR, New York City, by invitation.—Dr. Stohr presented lantern slides of three cases observed in the Woman's Hospital, in which a coincidence of granulosa-cell tumors and endometrial cancer was also noted.

Case 1 showed the uterus and appendages of a patient 64 years of age. The endometrium exhibited partial glandular hyperplasia and partial malignant degeneration of a mature type. The ovary contained a granulosa-cell tumor of massive form, composed of highly typical granulosa cells. This patient remained well during nine years of observation.

In Case 2, the slides were from curettings and an ovarian tumor of large size obtained from a 41-year-old patient. The curettings showed partly glandular hyperplasia and partly atypical proliferation with malignant characteristics. Some fragments were also present of a squamous cell mucosa presenting hyperproliferative excessive epidermization. The ovarian tumor was of the granulosa-cell variety, largely of massive type, partly of trabecular form.

Assuming the correlation between the neoplastic overgrowth of the endometrium and the ovarian tumor no radiotherapy was given. The reversibility of the endometrial changes was demonstrated by a microscopic slide of curettings obtained 6 weeks after the primary operation, which presented a normally built secretory mucosa. After this operation the menses continued in an entirely normal fashion.

In Case 3 the slides presented curettings of a patient 60 years of age with postmenopausal bleeding, showing partly glandular hyperplasia and partly papillary adenocarcinoma of marked maturity. The neoplastic tissue was particularly characterized by large plaques of squamous epithelial cells and cells in transition from the columnar to the squamous cell form. This case was first curetted, radiation therapy given and then 6 weeks later as a routine measure, complete hysterectomy and bilateral salpingo-oophorectomy were performed. The microscopic slides of the operative specimen present an ovarian tumor 3 cm. in diameter, a typical granulosa-cell tumor of mature follicular type.

In reviewing these three cases one may arrive at the theory that a direct correlation exists between the maturity of the granulosa-cell tumor and the carcinogenic effect. While the immature form of the granulosa-cell tumor (first two cases) exerted less carcinogenic activity, the mature follicular form (third case) produced the more pronounced and immature form of endometrial carcinoma.

DR. EMIL NOVAK, Baltimore, Md.—We also have encountered a number of cases in which adenocarcinoma of the uterus has been found in association with granulosa- or theca-cell tumors of the ovary, but I shall not stop to detail them here. When such an association is found, one must think of the so-called combined types of cancer, in which two different varieties of cancer are found in one or more organs. It is unlikely that this factor of coincidental coexistence applies to the group of cases illustrated by those just reported by Dr. Ingraham. It is significant that while a considerable group of this variety has been observed, granulosa-cell carcinoma has also been reported with carcinoma of the breast, but not with cancer in other organs. This would seem to bear out the generalization laid down many years ago by Loeb, to the effect that estrogen may play some role in the development of cancer, but only of those organs and tissues which are normally under the physiologic control of estrogen.

It should be remembered that granulosa-cell carcinoma of the ovary rather characteristically provokes a hyperplasia of the endometrium, and that in some cases of the latter, a proliferative picture may be found which could be mistaken for cancer, although it is perfectly benign. Indeed, I would be inclined to interpret in this way one or two of the slides which Dr. Stohr has thrown on the screen as adenocarcinoma, although I appreciate the hazard of microscopic diagnosis from a single lantern slide.

Some years ago Taylor and his associates, and shortly afterward Yui and I, published studies to emphasize the relatively frequent association of postmenopausal hyperplasia and adenocarcinoma of the uterus. I still feel that this finding is of significance, and that the subjection of the postmenopausal endometrium to estrogenic stimulation may play at least a predisposing role in the development of cancer.

DR. INGRAHAM (closing).—We do not mean to be too dogmatic in saying whether these cases were carcinomas or hyperplasias, but I think from histologic specimens it would be impossible to say that they were not endometrial carcinomas.

Dr. Frank Pemberton, who was to discuss this paper, said they had had at the Free Clinic for Women, in Boston, seven cases of a combination of ovarian tumor with adenocarcinoma of the corpus uteri. In one case the accompanying ovarian neoplasm was a granulosa-cell tumor; in five a theca-cell tumor and in one a luteoma. I think that perhaps this is a more common association than we perhaps realize. We feel that the condition is secondary to the theelin stimulation accompanying the granulosa-cell tumor.

THE MINIMAL HISTOLOGICAL CHANGES IN BIOPSIES TO JUSTIFY A DIAGNOSIS OF CERVICAL CANCER*

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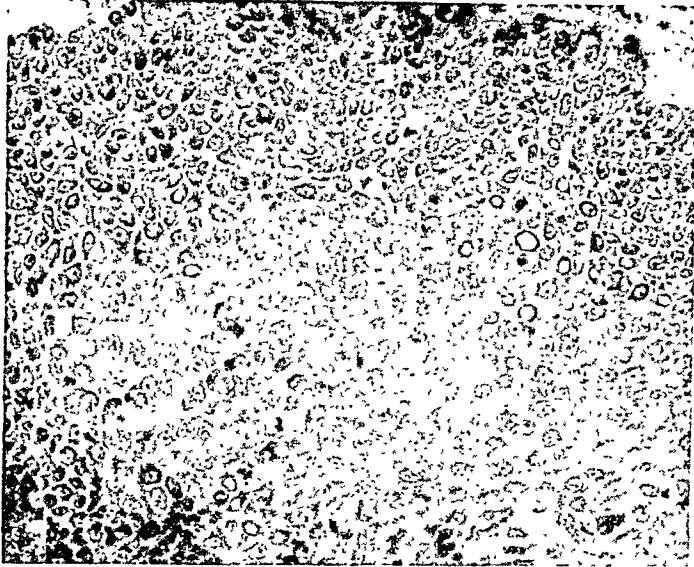
(From the Gynecological Department of the Johns Hopkins University and Hospital)

THE minimal histological epithelial change in the cervix required to justify a diagnosis of carcinoma presents a problem about which there is still considerable controversy among gynecological pathologists. The inability of pathologists to diagnose with certainty extremely early lesions has resulted in many mistakes of a serious nature. Errors are made in both directions. Benign cancerlike lesions, the result of squamous cell metaplasia and epidermidization are frequently erroneously called malignant. Early malignant lesions are also not infrequently erroneously considered benign. Often, when dealing with these cancerlike lesions, the pathologist is in doubt, and he attempts to mask his lack of knowledge by calling them "precancerous." This results in unnecessary surgery or irradiation. It is not, however, with these cancerlike lesions that we are concerned in this paper. For a consideration of them, the reader is referred to articles by Novak,¹ Meyer,² and TeLinde.³ In this study, we have interested ourselves in the extremely early malignant lesions which are not infrequently called benign at a time when they could be cured by surgery or by irradiation. In the present study, we have attempted to call attention to the earliest histological changes found in biopsies which have, in these cases, constituted the warning signal which has led us to the ultimate diagnosis of cancer.

One or more biopsies were taken from all of the cervixes of this series. In approximately half of the cases, several well-trained gynecological pathologists were unwilling to make the diagnosis of cancer from the changes noted in the biopsy specimens. We, too, confess that there was doubt in our minds as to the true malignant nature of some of the biopsy specimens, but since in many of the cases hysterectomy was indicated because of fibroids or functional bleeding, it was easy to make the decision to perform a total hysterectomy. In all instances the entire cervix was cut into blocks, and in many cases much careful searching had to be done before an area of actual invasion was found. A correlation of the biopsy findings with the ultimate histopathological findings in the removed cervixes was made.

In ten of the series of eleven cases to be presented here, we found, after removal of the cervixes, absolute histological evidence of invasive car-

*Read at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.



A.



B.



C.

UNIVERSITY OF WASHINGTON
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Fig. 1.—See page 776 for case history legend.

cinoma. In the eleventh case, the only area of invasion was found in a biopsy specimen, but the removed cervix showed extensive changes in the surface epithelium such as were seen in the biopsies of the other cases. The results of the study have been illuminating to us and, we believe, should prove of value in interpreting future biopsy specimens.

We are presenting below brief résumés of the clinical and pathological facts concerning these eleven cases. In none of these women was a diagnosis of cancer possible from palpation or inspection of the cervix. In only one instance was any ulceration seen. The biopsies were taken because of slight suspicion on inspection of the cervix, because of a history of intermenstrual spotting, with or without a suspicious-looking cervix, and, in a few instances, as a matter of "routine" when curettage was done. In one instance, the lesion was discovered accidentally in the routine histological examination of a normal-appearing cervix which was removed in the course of a Manchester operation for prolapse.

Discussion

From a study of this material we have concluded that the abnormal cellular activity which eventually results in fully developed cancer begins in the basal cells of the surface epithelium. In the normal cervical epithelium there is a single layer of fat spindle cells forming the basal layer. They stain deeply with hematoxylin. (Fig. 12, *C*.) The transition from this normal picture to extreme basal-cell hyperactivity involving the full thickness of the surface epithelium may be shown histologically

Fig. 1.

CASE 1.—History No. 170,677. Path. No. 48793; 49,533 and 49,633. Aged 30 years. Para 0. Complaint: Intermenstrual bleeding.

Biopsy taken on July 12, 1939, because of granular appearance of cervix. Section (Fig. 1*A*) showed marked basal-cell hyperactivity of the surface epithelium with many mitotic figures. No invasion. Patient observed. Second biopsy (Fig. 1*B*) taken on November 30, 1939, because of postcoital spotting, showed complete loss of stratification of surface epithelium and definite invasion of cervical stroma by histologically similar epithelium. Definite diagnosis of carcinoma was made and total hysterectomy done on December 22, 1939. Entire cervix cut in blocks and sectioned. Only beginning invasion was found at one point (*C*), but surface epithelium showed extensive change as in first biopsy. Apparently only area of unquestionable invasive carcinoma was excised at second biopsy (*B*).

Fig. 2.

CASE 2.—History No. 152,017. Path. No. 52,721; 52,751 and 52,820. Aged 28 years. Para 0. Complaint: Profuse and prolonged menses for 6 months.

No intermenstrual bleeding. Leucoplakic area on cervix biopsied on June 11, 1941 (Fig. 2*A*), showing small piece of epithelium with complete loss of stratification. Because of plane of section and inflammation, it was difficult to orient section. Second biopsy taken on June 16, 1941 (*B*), showed only basal-cell hyperactivity; no invasion. Total hysterectomy, left salpingo-oophorectomy done on June 25, 1941. Total cervix sectioned revealing definite invasive carcinoma with partial destruction of gland (*C*).

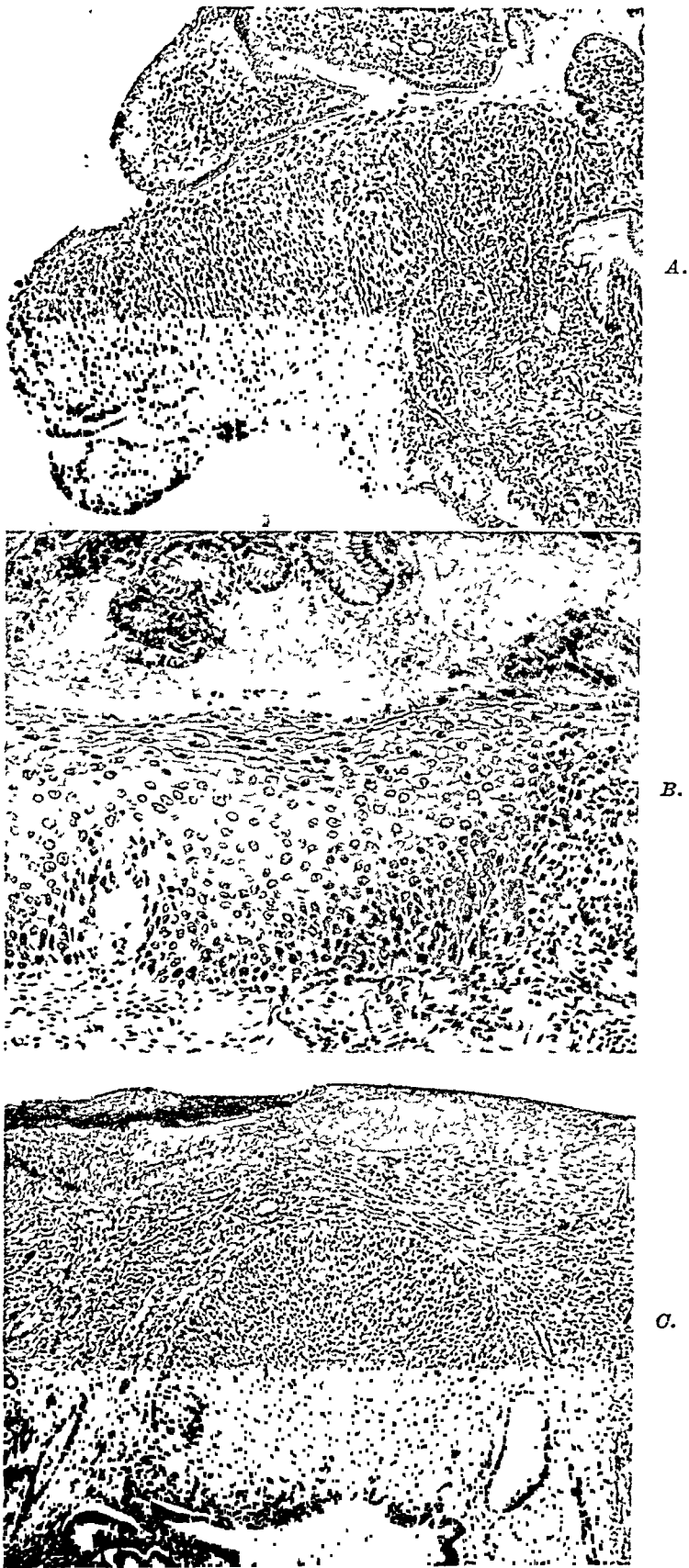


Fig. 2.—See opposite page for case history legend.

in a variety of ways. The normal and hyperactive epithelium may be demarcated by the often-described short oblique line of Schiller. We have observed more often, however, a gradual transition from slight overactivity to a complete involvement of the full thickness of the epithelium by hyperactive epithelial cells. Figs. 12, *A* and *B* show this overactivity. At the left of section *A*, the full thickness of the epithelium is taken over by the hyperactive basal cells. In some instances, as one follows the increase in basal-cell proliferation along the surface epithelium, a long sharp oblique line may be seen demarcating the hyperactive basal epithelium from the upper normal epithelium. (Fig. 3 *C*.) On the other hand, we have rarely observed an absolutely abrupt change indicated by a perpendicular line as shown in Fig. 13. Regardless of the manner of transition, when the full thickness of the epithelium is made up of this hyperactive basal epithelium, the ultimate picture is the same. There is a complete loss of the normal stratification of the cells; the cells and especially the nuclei are irregular in size and shape, and a variable number of mitotic figures are present.

It would seem from our observations in tracing these surface changes that after the hyperactive basal epithelium has taken over the full thickness of the epithelium, the next step is invasion of the subepithelial tissue. So frequently have we traced this succession of histological changes that there is a strong suggestion that this is actually the succession of events. The glands seem to afford a favorite route for invasion of the underlying tissue. The columnar epithelium lining the gland is destroyed as the epithelium advances. When the base of the gland is reached, the malignant epithelium continues its growth into the depth of the tissue. There is a distinct difference between this process and that seen when the columnar lining of a gland is replaced by the benign process of epidermidization. Aside from the difference in character of the individual cells taking part in invading the gland, there is the difference that when the lumen of the gland is filled in its length and breadth by the epidermidization process the growth ceases, whereas the malignant growth continues into the adjacent tissue.

From our observations in the afore-mentioned eleven cases, there is the strong suggestion that all epidermoid cervical cancer arises in the basal-cell layer regardless of what cell type predominates ultimately in the fully developed cancer.

Fig. 3.

CASE 3.—History No. 96816-2 U.M. Path. No. 54,007; 54,048; 54078 and 54,153. Aged 31 years. Para 0. Metrorrhagia January to May, 1941.

Spotty leucoplakia of cervix. Biopsy on January 13, 1941 (Fig. 3*A*), showed only marked basal-cell activity. Cervix amputated on January 26, 1942 (*B*), showed some hyperactive epithelium on surface and invading deep into subepithelial tissue. Section from surface of cervix elsewhere showed long oblique line demarcating various degrees of basal-cell hyperactivity from upper hornified layer (*C*). This is not the usual short oblique line described by Schiller.

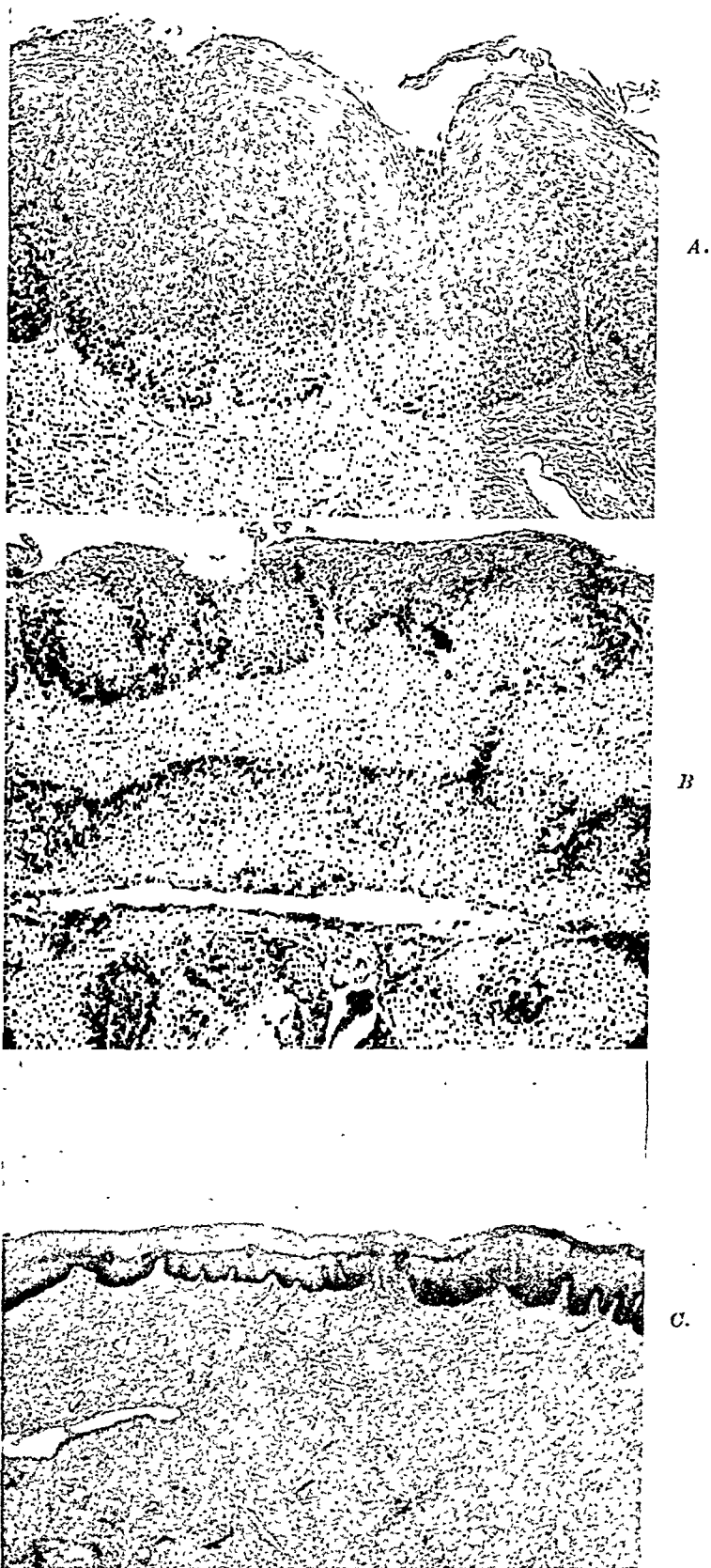


Fig. 3.—See opposite page for case history legend.

The question of how long such surface epithelial changes can be present before actual invasion takes place, or indeed, whether such surface changes inevitably develop into true invasive cancer is of great

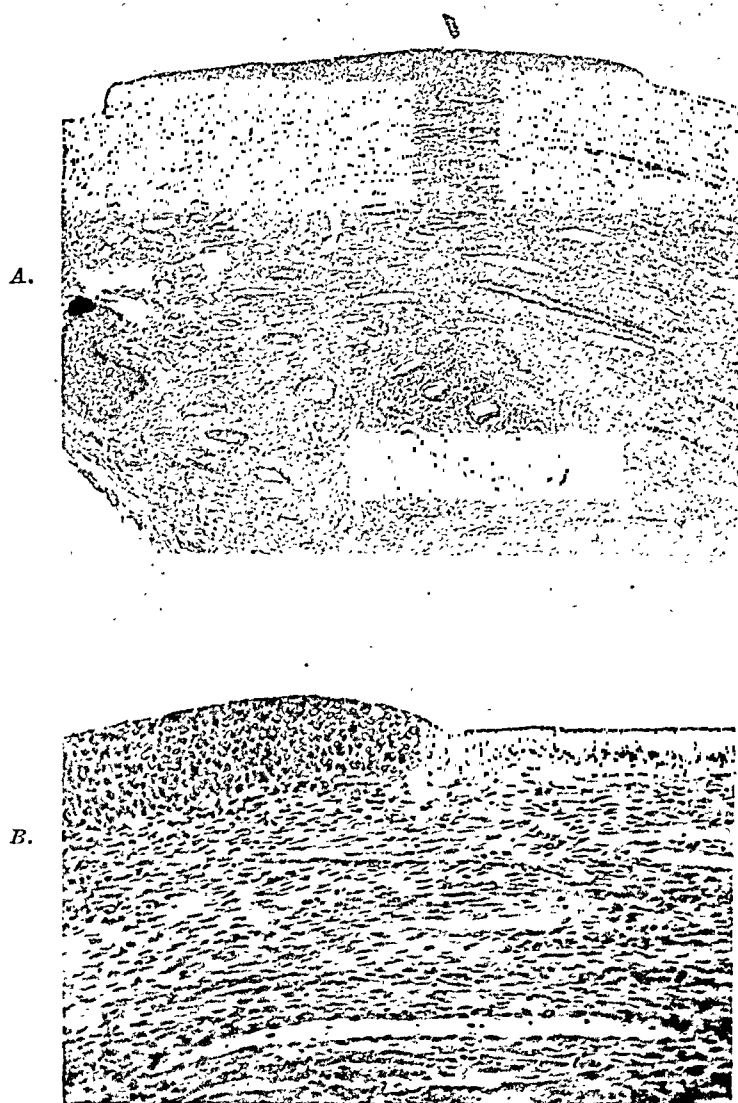


Fig. 4.

CASE 4.—History No.116,807. Path. No. 54,653; 54,688; 54,736; 54,809. Aged 31 years. Para 1-1. Metrorrhagia for one month.

Cervix very firm with hypertrophied anterior lip and small bleeding points near external os. First biopsy taken April 28, 1942 (Fig. 4A), showed complete loss of stratification at external os and a small bit of invasive epithelium of a similar character. High power of surface epithelium directly at junction of columnar and stratified epithelium (B). Subsequent biopsy taken on May 5, 1942, showed normal cervical tissue. A third biopsy taken May 14, 1942, showed surface epithelial change similar to that of first biopsy but with questionable invasion. On May 27, 1942, a total hysterectomy and double salpingo-oophorectomy were done. Sections of cervix (C and D) showed same surface changes and also definite invasion, destroying glands in depth of cervix.

scientific interest and clinical importance. It is interesting to note that the average age of these 11 cases of extremely early cancer is only 36 years, in contrast to an average age of 48 years for cancer of the cervix in general. This suggests, at least, the possibility of a surface lesion existing for years before the development of a gross carcinomatous lesion. We have, in our laboratory, two cases on record which cast some light upon this question. They have already been recorded in the literature by Stevenson and Scipiades.



Fig. 4.—See opposite page for case history legend.

C. P.—K 13414. Path. No. 25,171. Aged 28 years. Para 4-4. Trachelorrhaphy June, 1919. Routine examination of tissue removed showed noninvasive changes in surface epithelium similar to that seen in the present series. Speculum examination 2 years later showed cervix covered with normal-looking epithelium. Examination February, 1928, showed a large cauliflower-like carcinoma of cervix. Microscopic diagnosis: epidermoid carcinoma.

M. S.—Path. No. 49,900; 41,429 and 45,520. Aged 34 years. Complaint: dyspareunia. Routine speculum examination showed slight reddening about external os. Biopsies taken from that region on July 31, 1934, showed noninvasive carcinoma-like change in surface epithelium. Patient refused treatment. Second biopsy taken January 8, 1935. At this time cervix looked normal. Biopsy again showed some changes in the epithelial surface. Treatment refused. Death July 15, 1937, from pernicious anemia. Had no symptoms of carcinoma of cervix. Cervix removed after death showed extensive changes in surface epithelium similar to that noted in biopsies but invasion into stroma of cervix was seen at many points. No autopsy was obtained so further extension of carcinoma could not be determined.

In the first of the above cases, we have a definite record of typical surface epithelial changes $8\frac{1}{2}$ years before the patient finally developed an extensive cauliflower-like cervical cancer. In the second case, the surface epithelial changes were known to have existed for three years before death from pernicious anemia. Up to that time no clinical evidence of carcinoma had developed, but the microscopic examination of the entire cervix showed undoubted invasive cancer. It cannot be stated how long the surface epithelial changes may exist before invasion begins, but the above two cases suggest the possibility of a duration for years. One cannot say with certainty whether invasion is eventually inevitable when such surface lesions exist. Since the two afore-mentioned cases illustrate that these lesions may exist for years before the development of clinical carcinoma, it is probable that in some cases death may take place from other causes before true invasive carcinoma develops.

In this connection it is important to know whether, after identifying the typical surface lesion, one is justified in proceeding with radical treatment in each case. In the past year, after finding these typical surface epithelial changes in biopsies, we have failed twice to find evidence of invasion on making a careful search in the removed cervix. Are we to regret these two hysterectomies as unnecessary operations? We believe not, in view of the findings in the foregoing reported eleven cases. Although we cannot say with absolute certainty that invasion would

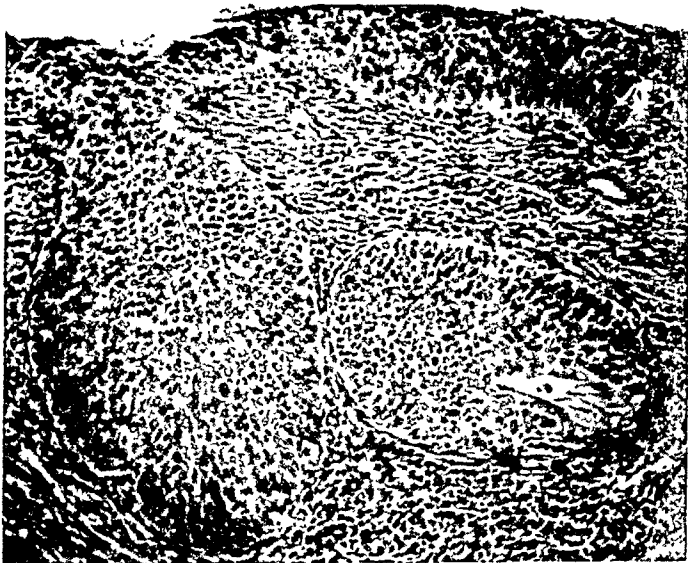
Fig. 5.

CASE 5.—History No. 254,539. Path. No. 54,437; 55,479; 55,494. Aged 30 years. Para 7-7. Menorrhagia since January, 1942.

Dilatation and curettage September 16, 1942; curettings showed endometrial hyperplasia. Cervix showed a little roughening about external os and that area was biopsied at time of dilatation and curettage. Biopsy (Fig. 4A) showed complete loss of stratification in one small area. Total hysterectomy was done because patient was a severe functional bleeder. Sections (B and C) from cervix show undoubted invasive carcinoma. Section (C) shows marked contrast between early cancer on the left and epidermidization on the right.



A.



B.



C.

Fig. 5.—See opposite page for case history legend.

A.



B.



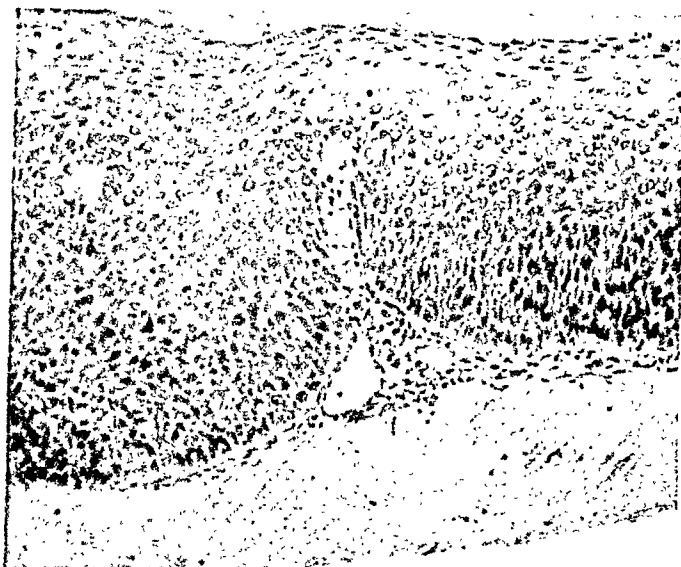
Fig. 6.

CASE 6.—History No. 156,130. Path. No. 55,853; 55,869. Aged 39 years. Para 6-4. Postcoital spotting for two to three months; profuse bleeding 3 days.

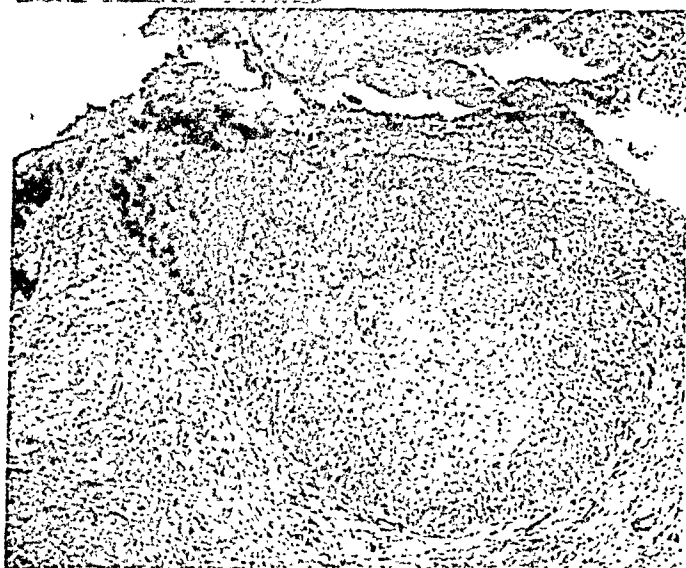
Myomatous uterus; soft granular cervix about external os. Biopsy of cervix taken November 16, 1942 (Fig. 6A), showed only surface epithelium with complete loss of stratification. Total hysterectomy November 18, 1942. Cervix showed definite invasive carcinoma. Many tongues of invasive carcinoma are shown under low power in B.

CASE 7.—History No. 277,430. Path. No. 55,695; 55,811; 55,890 and 55,947. Aged 39 years. Para 6-4. Complaint: Profuse menses for one month. No intermenstrual bleeding.

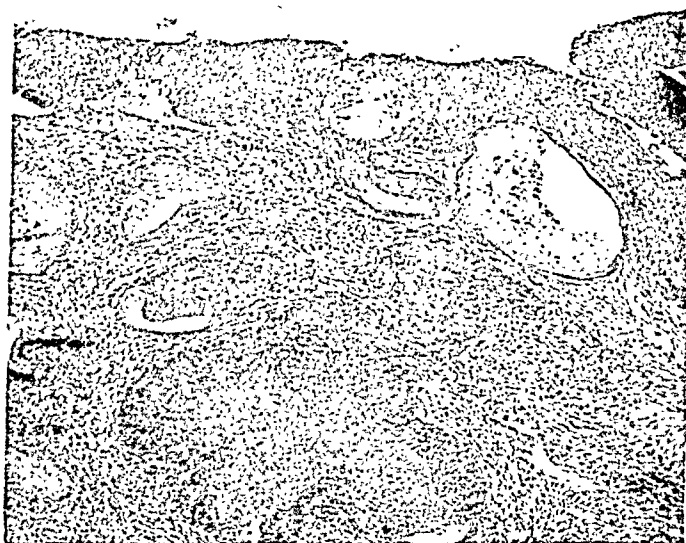
Myomas present. Cervix firm, lacerated with irregular, hypertrophied anterior lip and granular posterior lip. Biopsy taken October 20, 1942 (Fig. 7A), showed marked basal-cell hyperactivity but no invasion. Biopsy taken one month later (B) showed a tangential section through hyperactive basal epithelium. Section from cervix, removed by total hysterectomy December 3, 1942, showed definite invasive carcinoma (C).



A.



B.



C.

Fig. 7.—See opposite page for case history legend.

have eventually resulted in these two cases, we believe that there is a strong likelihood, and regard the surgery as justifiable prophylaxis. It is our considered opinion that when basal-cell hyperactivity is of such a degree as to involve the full thickness of the epithelium, replacing the normal stratified epithelium, hysterectomy is indicated. Since all degrees of basal-cell hyperactivity are encountered, there will be inevitably some instances in which there will be doubt as to the proper procedure. A good working rule in cases in which the hyperactivity is of a questionable degree is never to lose sight of such a patient, but to biopsy and re-biopsy at intervals of a month or two until one is quite satisfied that he is or is not dealing with early malignancy. The question can usually be answered quite definitely within a few months.

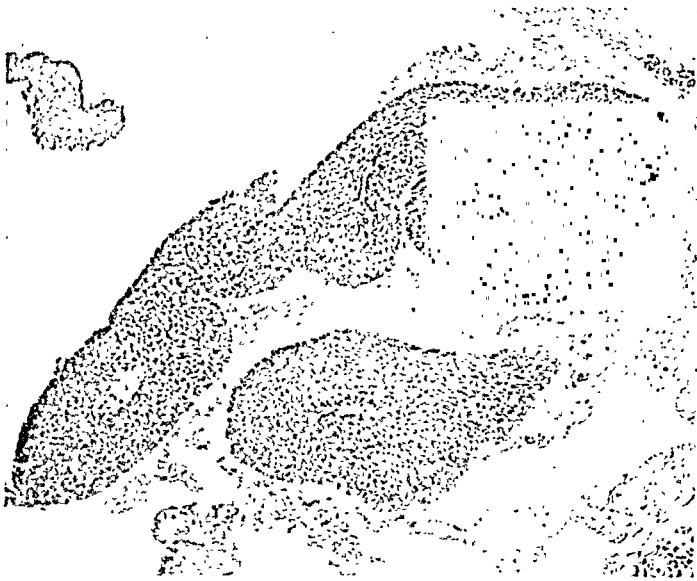
From a review of these cases, it becomes obvious that the diagnosis of early cervical cancer has become a matter of appreciation of the finest and earliest changes in the epithelium. In our present state of knowledge, we do not know enough about these early changes to be dogmatic concerning the exact degree of epithelial change necessary to justify a diagnosis of cancer, but in this report we have recorded eleven cases in which the change in the surface epithelium was sufficient to cause us seriously to suspect carcinoma. Unquestionable cancer was found on complete section of the cervix in ten cases. In the eleventh, invasive carcinoma was seen in one biopsy section. These cases stress the importance of biopsy and often repeated biopsy of cervixes of which one is suspicious either on the basis of the history of spotting and/or the appearance of the cervix. These cases also stress the fact that the most vulnerable spot for the beginning of cervical cancer is the external os, or more exactly, at the junction of the squamous and columnar epithelium.

In some instances in which the history of spotting causes one to be suspicious, and yet when the appearance of the cervix gives no clear-cut indication of where the biopsy should be taken, tissue had best be excised at the external os. In one of the foregoing cases, the first biopsy was only suspicious; a second biopsy was taken by doing a conization and completely sectioning the cone of tissue. Although we have not used conization extensively, because most of these biopsies were taken in the outpatient department, we believe that the procedure has merit at times, as a means of getting a complete biopsy of the vulnerable area.

Fig. 8.

CASE 8.—History No. 186,402. Path. No. 56,070; 56,081; 56,111. Aged 41 years. Para 8-7. Postcoital bleeding for 19 months.

Cervix hypertrophied with diffuse red and granular appearance of the posterior lip which bled easily on touch. Biopsy taken December 30, 1942 (Fig. 8A), showed only marked changes in surface epithelium; no invasion. Second biopsy taken December 31, 1942, showed similar changes. Total hysterectomy on January 6, 1943. Cervix showed same surface epithelial changes but also early invasive carcinoma (B and C).



A.



B.



C.

Fig. 8.—See opposite page for case history legend.

Because the changes are histologically of the finest type, we believe that the best possible sections should be utilized for study. For this reason, we never use quick-frozen sections in searching for these finer changes. In slightly over 24 hours an excellent paraffin-embedded and well-stained section can be made, and this slight delay is of no importance. It has never been shown that the lapse of a short interval of a few days between the time of the biopsy and subsequent treatment affects the prognosis adversely in cervical cancer.

The astonishing thing to us in making this study is the frequency with which these lesions have occurred in our laboratory. Eight of these eleven cases were found within a twelve-month period. During this time, 704 cervical biopsies were made. This incidence is much greater than has ever occurred in our laboratory during any corresponding period of time. The question arises whether such lesions have mistakenly been considered benign in former years. We believe that some errors have been made in this way, but probably the greatest factor in our increased finding of these lesions has been the great increase in the number of biopsies taken in our outpatient department and by our attending gynecologists in their private practice.

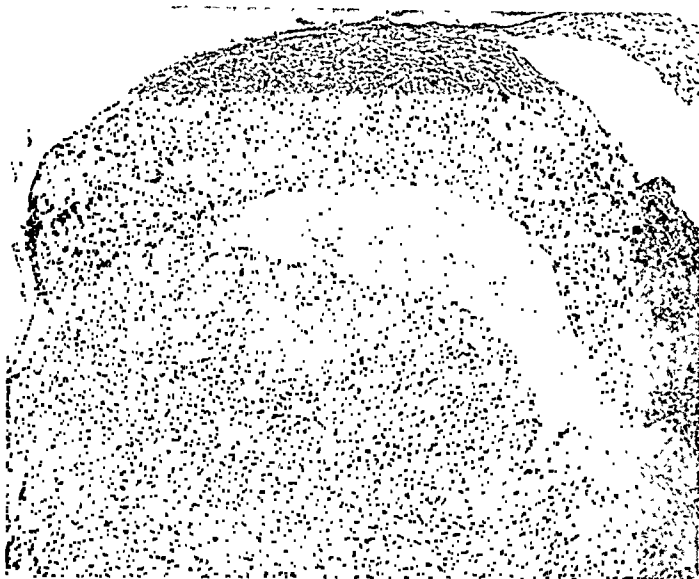
This paper was prepared for presentation before this Society at last year's meeting which was, as you all know, cancelled. We continued with this work during the intervening year and have discovered by biopsy five more cases which fall into the same category. This brings the total number of cases here reported to 16. In order not to lengthen the paper unduly, we have not reported the additional cases in detail or shown more photomicrographs.

The frequency with which we have encountered these lesions naturally has a direct bearing upon the choice between total and subtotal hysterectomy. Many factors beside the condition of the cervix enter into the decision in each case, such as the obesity of the patient, the general medical condition of the patient, the presence or absence of pelvic inflammatory disease, and the difficulties encountered at operation, but it is not within the scope of this paper to discuss this subject fully. We do wish, however, to put these data on record so that they may be evaluated in relation to the subject of total versus subtotal hysterectomy. The finding of 8 definitely cancerous lesions in normal or almost normal-looking cervixes in one year in a clinic in which 429 hysterectomies were done within the same period of time causes one to lean more toward total

Fig. 9.

CASE 9.—History No. 111,516. Path. No. 55,914; 56,108; 56,204; 56,257. Aged 33 years. Para 2-2. Postcoital spotting for 2 weeks.

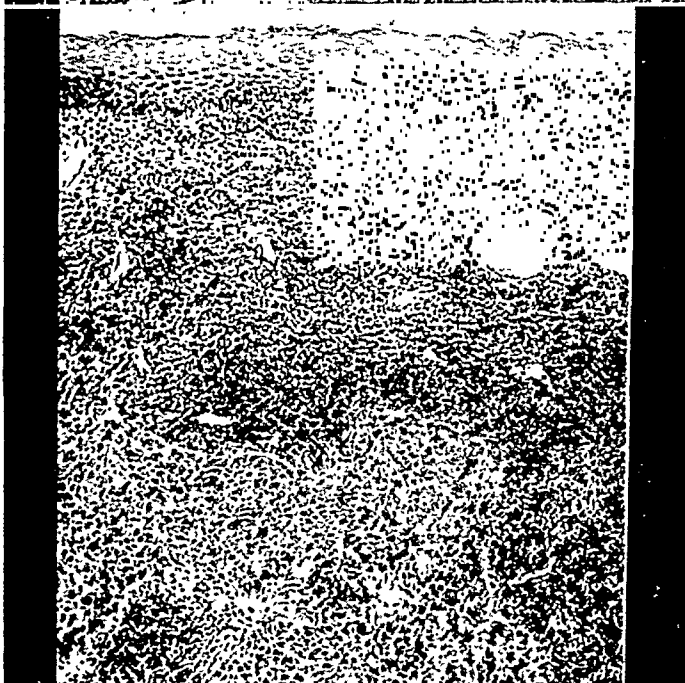
Cervix "large with shallow bleeding ulcer at 5 o'clock, the size of a small fingernail." Biopsy January 6, 1943 (Fig. 9A), showed complete loss of stratification and malignant change in cells but no invasion. Another biopsy January 20, 1943 (B), showed similar surface epithelial changes. Hysterectomy January 27, 1943. Cervix showed undoubted deep-lying carcinomatous tissue (C). This is the only case in which the carcinoma actually lay in the portio away from the external os and undermined normal mucosa.



A.



B.



C.

Fig. 9.—See opposite page for case history legend.

A.



B.



Fig. 10.

CASE 10.—History No. 160,962. Path. No. 56,470; 56,583; 56,603. Aged 39 years. Para 2-0. Complained on March 15, 1943, of amenorrhea since November.

Leucoplakic area seen on cervix. Biopsy showed suspicious areas in surface epithelium (Fig. 10A). On March 16, 1943, conization of cervix was done. Cervical tissue removed, cut up entirely in several blocks, and further surface epithelial change seen as well as definite invasive carcinoma (B). Subsequent total abdominal hysterectomy was done. The remainder of cervix thus removed failed to show any more carcinoma.

hysterectomy. During the past several months, we have completely cut into blocks all the cervixes removed by total hysterectomy and cut many sections from each block. We now have carried out this laboratory procedure in 240 instances. Among these, we have encountered microscopic extremely early invasive carcinoma in two instances. Often it was necessary to cut a great many sections before the area of invasion was found. In every one of these cases we had satisfied ourselves by history, cervical inspection and/or biopsy that cancer did not exist before operation and yet the removed cervixes showed cancer in 1.3 per



Fig. 11.

CASE 11.—History No. 285,228. Path. No. 56,452. Aged 49 years. Para 2-2. Complaint: On July 24, 1941, complained of heavy sensation in pelvis.

Pelvic examination showed cystocele, rectocele and descensus of uterus, almost second degree. February 25, 1943, Manchester parametrial fixation done. Cervix not suspicious of malignancy. On routine examination of cervix in laboratory, intra-epithelial changes were noted in surface epithelium (Fig. 11A). Entire cervix was then cut in blocks and sectioned. Invasive carcinoma was found (B). Patient was treated with irradiation.

cent. This finding of even an occasional cancer in normal-looking, asymptomatic cervixes, some of which were biopsied, is rather startling. It undoubtedly indicates the desirability of getting rid of the cervix, but it does not dictate the policy of routine total hysterectomy in complete disregard of the other factors mentioned above. Certainly, it behooves the gynecologist who performs subtotal hysterectomy frequently, to biopsy freely all cervixes on the slightest suspicion.

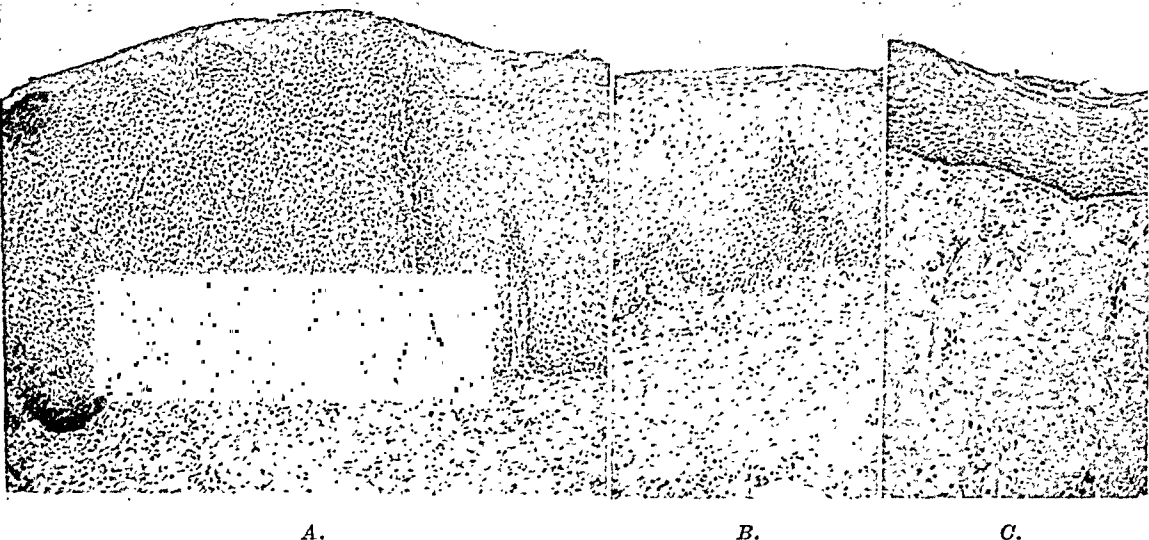


Fig. 12.

CASE 11.—*A.* Normal cervical epithelium, with single layer of fat spindle cells at base.

B. Increased basal-cell proliferation.

C. Still more marked basal-cell proliferation. As one progresses from right to left, the basal-cell hyperactivity increases until finally the full thickness of the surface epithelium is taken over by the overactive basal cells.



Fig. 13.

CASE 11.—Abrupt transition from normal epithelium on the right to hyperactive epithelium on the left.

Treatment

It is not the purpose of this paper to advocate surgery rather than irradiation in these extremely early carcinomas. Our attitude toward the treatment of carcinoma of the cervix, in general, is that all lesions of macroscopic size should be given a full course of radium and x-ray therapy. In these very early microscopic lesions, we believe that no one has had sufficient experience to be dogmatic in his preference for either surgery or irradiation. It is probable that the incidence of cures will be high by either surgery or irradiation. In our series, we have performed total hysterectomy in all cases except one. This one exception is the case in which the cervix was amputated in doing a Manchester operation. Following the discovery of early carcinoma in the amputated cervix, irradiation was instituted. We have favored surgery in order to obtain the cervix for study so as to substantiate or disprove our suspicion of cancer. Without doing this, we would still be in doubt as to the absolute diagnosis in several of the afore-mentioned cases. We have also favored hysterectomy in order to learn whether these early lesions can be cured with the conservation of one ovary. The average age of these patients is 36 years, and they are not rare in the twenties. The preservation of a functioning ovary in the younger women of this group would give surgery a decided advantage over irradiation. Since the ovaries are involved in cervical cancer late in the course of the disease, it seems probable that ovarian preservation will prove permissible in this group of cases.

The operation which we have carried out is a marked modification of the Wertheim technique. We do not hug the cervix as in total hysterectomy for benign disease. On the other hand, we make no dissection of the glands. If on examination of the removed uterus the lesion is found to be more extensive than originally suspected, we would entrust the destruction of possible glandular metastases to postoperative irradiation. We have frequently passed ureteral catheters preoperatively in order to facilitate the locating of the ureters at the operating table. This procedure requires but a few minutes either before or after anesthetizing the patient, and often proves to be of great value to the operator. The ureters can be identified easily and repeatedly in the course of the operation, permitting ligation of the uterine vessels well away from the cervix, and the removal of a generous vaginal cuff without endangering the ureters as they turn forward anterior to the vagina. Dissection of the ureters as in the typical Wertheim operation becomes unnecessary and thus postoperative ureteral fistulas never occur.

All of the 16 cases reported herein are well, but that fact is of no statistical significance since the longest time that has elapsed since hysterectomy is four years. The patients will be followed with great care to learn the ultimate results.

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Discussion

DR. GEORGE H. GARDNER, CHICAGO, ILL.—If anyone doubts the nature of these lesions, may I assure him that they are undoubted carcinomas of the cervix. Dr. TeLinde and Dr. Galvin have had an unusual experience with these early squamous cell cancers of the pars vaginalis, chiefly because they are continuously searching for them. I, on the other hand, have seen only a half dozen similar cases.

Their observation that the first evidence of cancer occurs in the basal layer of cells has not been confirmed in my specimens. Nevertheless, I do subscribe heartily to the concept that squamous cell cancer of the cervix can be diagnosed before actual invasion occurs. Such a diagnosis is based on radical alterations in the normal architecture of the squamous epithelium, plus individual cell changes, i.e., variations in the size, shape and intensity of staining of cells, plus mitotic figures. This type of cancer is, in reality, an intraepithelial process. Incidentally, it is sometimes difficult to be absolutely certain that early invasion has actually occurred.

We must be willing to diagnose cancer on the basis of cell changes alone, and then have the fortitude to treat the patients accordingly. I cannot subscribe to the practice of repeated biopsies as a follow-up in women where evidence of intraepithelial cancer is discovered, but cancer is not diagnosed because invasion has not occurred. One must look upon repeated biopsies as repeated traumas to the cervix.

Another of the authors' observations emphasizes a fact that may prove startling to some, viz., that slow growth of cancer is probably the rule, not the exception. They mention the youth of their patients and also cite a case that had been reported from the Johns Hopkins Clinic, in which almost nine years elapsed between the recognition of noninvasive intraepithelial cancer, and the appearance of a classical evverting clinical cancer of the pars vaginalis.

In this connection I wish to comment on another feature of some uterine carcinomas, viz., their tendency to spring up, apparently simultaneously, in several areas, or over an extensive surface, rather than being restricted to a single focus.

I must question one of their indications for treating these early invasive cancers by operation. They recommend that it is advantageous in younger women to save a functioning ovary. Few of us believe that estrogens in therapeutic dosage have a carcinogenic action, but some of us carefully withhold estrogens from cancer patients. The castrated woman, under treatment for genital cancer, who complains of hot flashes, probably should not be treated with estrogenic hormones. If Dr. TeLinde prefers to operate on his cancers of the cervix, I sincerely trust that he has other, and more valid, indications for surgery than the desire to avoid an early menopause. It is not at all unlikely that women with genital cancer should be castrated, as an essential part of their treatment.

This timely paper is a boon to the proponents of routine total hysterectomy. It serves as another lethal argument against frequent use of the subtotal operation, and it should stimulate all of us to search more zealously for similar early cancers of the cervix.

DR. KARL H. MARTZLOFF, PORTLAND, ORE.—I would like to emphasize again Dr. TeLinde's general observation concerning the attitude of some toward those changes in the stratified cervical epithelium to which such appellations as "precancerous lesion," "carcinoma in situ," "Bowen's disease," "preinvasive cancerous change" or "noninvasive potential carcinoma" have been given. The ex-

pression "noninvasive carcinomatoid change" is, I believe, more realistic, for it tends to express the idea, that the lesion in question, while resembling cancer, may in fact not be a carcinoma. This I believe is important, for upon it hinges the decision as to one's further conduct toward such an afflicted patient. If this noninvasive change, and I am not now discussing Dr. TeLinde's major thesis, is regarded as an irreversible, progressive process, then patients so afflicted may be subjected to unnecessary surgery or radiation therapy. It is worth remembering that patients so afflicted have remained well for years when nothing more was done than local removal of tissue for diagnosis. A few of our own observations confirm this, but particularly pertinent are the studies of Stevenson and Scipiades.

I am in agreement with Dr. TeLinde that if one is to regard a given lesion as one probably associated with a coexisting but as yet undemonstrated cancer, then surgical removal (panhysterectomy) is the method of choice. This gives opportunity for study of the entire specimen and final decision as to the correctness of one's pre-operative estimation of the lesion. In no other way can a background of exact information be obtained.

I am dubious of the advisability of frequent removal of tissue for histologic study. I prefer, when the original biopsy reveals such a carcinomatoid change, either cervical amputation or preferably a wide conical endocervical enucleation combined with a low amputation utilizing the Sturmdorf flap principle. This accomplishes three purposes: the procurement of adequate tissue for intensive study, the avoidance of prolonged delay before arriving at a final decision, and the probable complete removal of suspicious pathological tissue when no cancer exists.

Finally, we come to the nucleus of Dr. TeLinde's study, viz., the re-evaluation of his preliminary histologic studies on the basis of the coexisting early cancer demonstrated only after the entire cervix became available for study. I would like to ask Dr. TeLinde what he considers as acceptable evidence of early bona fide invasion? Also may not the patient who developed full blown cancer 8½ years after a non-invasive carcinomatoid change was demonstrated have had an undiscovered bona fide cancer at the time of the original biopsy? Is it also not possible that this final manifestation of cancer may have been purely coincidental and that the cancer did not arise necessarily at the site of the previously demonstrated noninvasive carcinomatoid change?

I make these inquiries because Hinselmann and his proponents have repeatedly stated that cancer of the vaginal surface of the cervix arises on the basis of a pre-existing leucoplakia. However, up to the present time this has not been proved. In saying this I am not unmindful that coexisting leucoplakia and cancer have been reported, and I confess my sympathetic attitude toward the theory that bona fide cancer probably may develop from an area of noninvasive cancerlike change.

Dr. TeLinde's most pertinent observation is that all of the noninvasive carcinomatoid changes observed in his preliminary biopsies showed among other changes complete loss of cell differentiation and layer formation. It is therefore inferred, that these alterations may offer histologic evidence sufficient to warrant the assumption of a coexisting but unverified cancer. This is not only an interesting observation but one of great potential importance and one that, I am sure Dr. TeLinde will agree, requires confirmatory evidence.

In conclusion, it should be emphasized that these observations of Dr. TeLinde do not and are not intended to show that bone fide cancer originates in an area of noninvasive carcinomatoid change. More probably they illustrate the cytological changes that may occur in the stratified epithelium of the cervix where it impinges on established cancer producing what has been described as collateral cancer.

DR. NATHAN P. SEARS, SYRACUSE, N. Y.—Since 1931, we have been carrying out a somewhat similar procedure. When any specimen of cervix is obtained showing a lack of stratification, the patient is put on a special list and frequently examined, sometimes as often as every month, in other cases every six months or a year. We

have picked up two cases after a year, and some diagnoses were confirmed within a month or two after our first suspicious biopsy was made. In this way, we will be able to detect a great many more of these cases, and therefore prevent deaths from cancer of the cervix.

DR. EMIL NOVAK, BALTIMORE, MD.—Year after year, before this Society and before practically every other gynecological society, there are discussions as to the treatment and the results of treatment for cancer of the uterus. While improvements are from time to time noted, they are on the whole unimpressive, and no one is particularly enthusiastic about them. For the present the only avenue to better results, and an obvious one, is through a combination of popular education and a more intensive and concentrated study of the cervix, in an effort to unearth the very early cases which will yield a very high percentage of cures.

The most important lesson to be drawn from Dr. TeLinde's paper is that one should go slowly in diagnosing preinvasive carcinoma. In almost all of his cases, in which definitely cancerlike changes were found at biopsy in the surface mucosa alone, without invasion, later biopsy or hysterectomy revealed invasiveness at some point or other. It is true that a small group of cases has been reported in which even serial study has failed to reveal invasion, and concerning the significance, the nomenclature and the treatment of this group, there has been much discussion and much difference of opinion. But these cases are far less numerous than those which, on more intensive study, reveal invasiveness, so that the diagnosis of cancer would be accepted by all pathologists. To put it another way, one would not make any mistake if one considered as cancer all those cases of extreme cancerlike changes in the epithelium even if the biopsy does not happen to show areas of outspoken invasion.

The rub in the situation lies in the determination of what constitutes a minimum of epithelial hyperactivity on which to base the assumption of cancer, for all degrees are encountered, as exemplified in the various rubrics of leucoplakia described by Hinselmann. The lesser degrees represented by rubrics I and II are probably of no significance, and it is only the rubric III cases, corresponding to those shown by Dr. TeLinde today, that one is justified in grave suspicion. In most biopsy sections corresponding to this picture, more extensive study will, as already mentioned, reveal invasiveness at some point, so that they will probably be placed in rubric IV, or genuine and undoubted cancer.

As for minor degrees of hyperactivity, they are probably of no significance in relation to cancer. In interpreting them we must consider individual variations, the influence of inflammatory irritation, and possibly cyclic or other endocrine variations. The vaginal mucosa is much influenced by hormone factors, and there would seem to be no reason why the same thing should not apply to the squamous epithelium of the portio, although we have very little direct information on this point as yet.

DR. I. C. RUBIN, NEW YORK CITY.—In 1910 I was able to report three cases of what we called at that time "incipient" cancer of the cervix. These cervixes were removed from cases of uterine prolapse at the von Rosthorn Klinik. The lesions corresponded to those this morning, and to those which Dr. Cullen showed some twenty years later. At that early period Schottlaender, pathologist at the von Rosthorn Klinik, was alone in maintaining that the mitotic activity of the cells, loss of the basal-cell arrangement with local regional and some subjacent lymphatic involvement underlying the proliferated hyperactive epithelium, without any further spread, was enough to characterize the lesion as cancer. I have seen several cases since that time, two of them since we have been doing the Fothergill operation more frequently, in which the rate of growth was extremely slow.

A woman in the late forties on whom I did a trachelorrhaphy with curettage had a lesion which corresponded quite accurately to this picture, one small fragment showing infiltrating squamous cell carcinoma (medium ripe). I urged the husband to

see to it that a hysterectomy be done or that she have x-ray or radium therapy, which he refused for fear of scaring her, since she had cancerophobia. I lost track of her for several years during which time she had estrogenic treatment receiving some 10 million international units of estradiol. When I saw her in 1943, some 7 years after the operation, her cervix was quite the same and perfectly healed. She still refuses to have anything done.

From what Dr. TeLinde's evidence shows in his beautifully carried out pathological examinations I think we are dealing in some of these cases with what is analogous to a basal-cell carcinoma. In other words, this lesion is an epithelioma of the vaginal portio which has relatively benign activity and for that reason may lie dormant and localize without producing remote metastasis for many years.

DR. F. H. FALLS, CHICAGO, ILL.—I want to emphasize what Dr. TeLinde has said as to the importance of removing the whole endocervix in operating upon these carcinomas. We do a Sturmdorf operation, excise the cone and open it out so as to make eight blocks. We start taking sections down the block and if we find nothing in the early sections, we assume that the cervix is negative. But if we find these early changes, the beginning Schiller line, we cut sections right through. We have made as many as 80 slides from one block finally to detect the carcinoma. The Sturmdorf operation is a good one for cervicitis quite apart from its advantages in detecting early carcinoma. Therefore, we believe that patients with chronic cervicitis that do not yield to ordinary treatment should not be treated by the cautery but by the Sturmdorf operation. This yields the best possible biopsy material.

After removing the early lesion by the Sturmdorf operation, the question is whether we are obligated to remove the uterus. That is hard to say. In a young woman of 24 or 25 years of age, we leave the uterus keeping the patient under close observation. If the patient is near the forty-year mark, we recommend the removal of the uterus. In some of these cases we have done the Schiller test before operating, have marked the point of the positive test and then after the Sturmdorf operation found that there was no invasion. A little beyond that point, however, we have found an early carcinoma, often where the Schiller test was negative.

DR. TELINDE (closing).—The question of repeated biopsy has been raised. I have seen no practical objection to it, and can see no alternative when one is in doubt from the first biopsy. We have coned the cervix only a few times, but believe it is a good way to get a very satisfactory biopsy. If one does this by the Sturmdorf technique, however, it is necessary to wait at least four weeks for the wound to heal, and all infection to disappear before proceeding with the total hysterectomy. If one were going to treat the patient with radium, one could start that therapy very soon after the conization.

Dr. Gardner raised the question of the advisability of saving one ovary when doing a total hysterectomy. We have discussed that question a great deal, but the effect of estrogen upon carcinoma is strictly theoretical, and we do not believe that we should be deterred from saving an ovary on theoretical grounds. We would not save an ovary in a woman past 38 years of age, but believe it is worth doing in the younger individuals. Dr. Martzloff brought up the question as to whether the patient who had a gross carcinoma eight years after the biopsy might not have had it long before that time. I think that is a possibility, but one cannot prove it.

In undertaking this study we appreciate that these intraepithelial changes have been described in the literature repeatedly. There seemed, however, to be one weak point in most of the published articles and that was proof of the relation of these surface changes to invasive carcinoma. We have attempted to prove this in these studies. I hope that we have stimulated a little interest in this subject, and I am glad that I have had the opportunity to present this paper at this time as it fits in so well with Dr. Macfarlane's work in her volunteer health checkups. I am sure that we were missing many of these early lesions before, considering the frequency with which we are finding them now.

THE SECOND STAGE OF LABOR—THE DESCENT PHASE*

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(From the Kansas University School of Medicine)

SOME years ago, we endeavored to demonstrate that the first stage of labor was a very simple process, controlled by the frequency and intensity of labor pains balanced against the resistance offered by the cervix.¹ The passenger, either with respect to its size or its presentation, had no effect on the progress of the first stage. With the possible exception of ruptured membranes, nothing other than labor pains and cervix was of any major importance.

A similar study of the second stage of labor reveals quite a different situation. Here, we find a very complicated process, affected by many different considerations. Voluntary effort of the patient is of as much, if not greater, importance than the involuntary contractions of the uterus. Ruptured membranes facilitate descent, but may act as a deterrent factor in negotiating the pelvic floor. Size of the passenger is of considerable importance, particularly in primiparas. Presentation is of little importance in some respects, but a definite factor as regards internal rotation. The station at which internal rotation takes place has a definite bearing on the rapidity and ease of delivery. The frequency and intensity of labor pains are of relatively little moment in multiparas, but a factor of considerable importance in primiparas.

Since there are so many factors involved and since these factors are more or less interdependent, clarity of understanding will be served by discussing only one of them at this time. The remainder of this discussion will concern itself with that phase of the mechanism of labor known as descent.

The textbooks give one the impression that descent, while partial in the first stage, is a more or less continuous process during the second stage of labor. In the present series of some, 2,400 primiparas and 1,700 multiparas, our findings are not quite in accord with this impression. In something over half (54 per cent) of all patients, the head was definitely on the pelvic floor at the time the cervix receded over the head. It has been our custom to say the cervix was completely dilated only when it was also completely retracted. Very frequently, there is no descent when the cervix is seemingly dilated but still palpably present around the head. Palpation at the height of the uterine contraction will show this remaining rim of cervix to be tightly clamped against the head and to be preventing descent thereof. As soon as the cervix is retracted, the head will frequently almost fall

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down through the pelvis to the perineum. Conversely, the head may be on the pelvic floor for a matter of minutes or even hours before dilatation is complete. The assumption that the patient is in the second stage of labor merely because the head is on the perineum may well lead to the impression that forceps delivery will be required because of "lack of progress." In these patients in particular, it is unsafe to depend upon the findings by rectal examination, and it has been our custom for the past few years to do vaginal examinations routinely under these circumstances (i.e., head on perineum with no progress).

In this group of patients, with the head on the perineum at the time dilatation is complete, the second stage is wholly concerned with the negotiation of the pelvic floor.

In the remaining patients (something less than half of all cases in the present series), the presenting point is at a somewhat higher station at the time dilatation is completed. This station may vary all the way from approximately 1 centimeter above the pelvic floor to a point well up in the pelvis. *In this latter group of patients, descent to the pelvic floor must precede the pelvic floor phase.* This descent may require all the way from a very few minutes to as much as an hour or more. After it is completed, there then remains the pelvic floor phase, which is exactly like the whole of the second stage in the first group of patients. It has seemed advisable to us when referring to the second stage in this second group of patients to speak of "Descent Phase" and "Pelvic Floor Phase." The duration of the second stage in this group cannot be directly compared with the second stage in the first group. Failure to make this differentiation inevitably leads to inaccurate judgments as to the proper amount of progress in individual patients and, therefore, to ill-advised abstinence from operative delivery in the first group and ill-advised early interference with the second group.

Etiology of High Station

Since more than half of all patients in this series had the head on the perineum at the time dilatation was complete, it becomes of interest to try to determine the etiology of the high station in the smaller group.

TABLE I. ETIOLOGY OF HIGH STATION
(AT ONSET OF SECOND STAGE)

| | |
|---|------------|
| Cervix and L.U.S. | 33% factor |
| Unruptured membranes | 15% factor |
| Large baby (over 3,500 Gm.) | 5% factor |
| Occiput posterior } | Negligible |
| Deflexion } | |
| Abnormal presentation, hydrocephalus, etc., not studied. | |

One major factor (the cervix and lower uterine segment), one somewhat less important factor (the time of rupture of the membranes), and

several almost negligible factors seem worthy of consideration. It is quite apparent that the cervix and lower uterine segment are much stretched and markedly thinned out before the onset of labor in a small proportion of patients. Some of these individuals are observed to "carry their babies on their heels" for the last several weeks of their pregnancies. Considerably more frequently, one observes the head descending through the pelvis during the first stage so that it may reach the pelvic floor by the time the cervix is only 5 or 6 centimeters dilated. Stretching of the lower uterine segment (and parametrial tissues?) would, therefore, seem to precede effacement and dilatation of the cervix in a small number of individuals, and to proceed apace in a considerable fraction of the remainder. Failure of stretching of the lower uterine segment and cervix would naturally prevent descent of the head until the cervix is completely dilated and, therefore, completely removed as an obstructive factor to descent. As nearly as could be judged from this present series of patients, 33 per cent of all individuals fall into this category. In this 33 per cent of patients, the station of the head is high at the time dilatation is complete regardless of all other factors in the individual.

The next most important consideration is the time at which the membranes rupture. Of 2,397 patients whose membranes had been ruptured previous to the completion of dilatation, 59 per cent (1,404 patients) had the head on the perineum at the time dilatation was complete. Of 1,185 patients in whom the membranes did not rupture until after the completion of dilatation, only 44 per cent (521) had the head on the perineum at the time dilatation was complete. That unruptured membranes can act as a deterrent to descent is particularly evident in multiparas whose pains are very poor, and who exert little or no voluntary effort. One patient in this series had complete dilatation for four hours with the head just above the pelvic floor and no progress. Rupture of the membranes was followed by birth of the baby within one minute and without a uterine contraction. The difference between 59 per cent and 44 per cent would suggest that late rupture of the membranes relative to the time of completion of dilatation is approximately a 15 per cent factor in preventing early descent.

Three other clinical findings were carefully studied and found to be unimportant or of negligible weight in determining station as of the time of complete dilatation. The presenting point in 52 per cent of primiparas was on the perineum, while in multiparas, 59 per cent was at a low station; 53 per cent of occiput anterior as against 51 per cent of occiput posterior; 55 per cent of the small and medium-sized babies and 50 per cent of the large babies (3,500 grams and over). Baby size alone, therefore, of these three factors might be considered as of minimum importance, and to be, at most, a 5 per cent factor. If we combine the factors favorable for a low station, namely, small and medium-sized multiparas' babies, with early rupture of membranes, we find that 66

per cent are on the perineum at the time the cervix is completely dilated; whereas, primiparas with large babies and unruptured membranes, have only 34 per cent on the perineum at the time the cervix is at complete dilatation. It is thus apparent that the resistance offered by the cervix is a very major factor in preventing early (first stage) descent; unruptured membranes are a considerable factor; and baby size, parity, and posterior occiput position are negligible—certainly so for the individual patient.

TABLE II. THE DESCENT PHASE

| | |
|------------------------|---|
| Voluntary effort | Most important |
| Character of pains | 20-minute factor |
| Large baby | 6-minute factor |
| Unruptured membranes | 3-minute factor |
| Occiput posterior | Negligible unless combined with other adverse factors |
| Late internal rotation | |
| Incomplete flexion | |

The Descent Phase of the Second Stage

The length of time necessary for, and the factors concerned in, descent occurring in the second stage are of considerable interest. (Table II.) Several factors are concerned with this process, but only two are of anything like major importance. It is not yet apparent whether the relative amount of voluntary effort exerted, or the relative intensity and frequency of the uterine contractions is the more important. It is quite apparent that patients with good pains coming at frequent intervals will bring about complete descent to the pelvic floor in an average of some twelve minutes in primiparas (multiparas—six minutes). Voluntary effort is unnecessary and relatively unimportant in this situation. On the other hand, if the contractions are quite weak and infrequent, good voluntary effort is almost a necessity and will frequently produce descent in ten to fifteen minutes. With average cooperation by the patient, descent requires an average of forty minutes, and with no voluntary effort may well require more than an hour. Since we do not have a precise method of measurement, we can only say that it is our present impression that voluntary effort is more important than uterine contractions, both with respect to the descent phase and the pelvic floor phase of the second stage of labor. This is more striking in multiparas than in primiparas.

Effectiveness of the uterine contractions can be somewhat more readily judged. Descent in primiparas with no obstructing factor and with good pains occurs in some twelve minutes. Where the pains are weak and infrequent, the pelvic floor may be reached in a few minutes, but may require forty minutes or more. The average in most such groups is thirty to thirty-five minutes. For purposes of comparison with the other factors involved, the labor pains could, therefore, be said to be a factor of twenty minutes or more.

Perhaps next most important is the size of the baby (occiput presentations only are being considered in this paper, and abnormal presentations are, therefore, automatically excluded). In primiparas, babies of 3,500 grams and over, require on the average some six minutes more for completion of descent (multiparas three minutes) than the average of small and medium-sized babies. Marked variations are observed, and it is not infrequent that large babies apparently descend more rapidly than small ones. These figures quoted are, therefore, to be looked upon only as averages or general tendencies. On this basis, largeness of baby could be said to be a six-minute factor.

In this group of patients, it was noted that if internal rotation took place during descent, that descent was completed on the average more rapidly than if internal rotation did not occur until after the presenting part was definitely on the perineum. Here again, the differential was about six minutes for primiparas, and three minutes for multiparas. This series is not sufficiently large for us to be certain whether this differential does not represent inadvertent selection. It may well be that some factor which inhibits internal rotation during descent also inhibits descent itself; as for example, the large size of baby above noted. In this connection, it was supposed by us that moderate degrees of deflexion would be found to be of considerable importance. Again, the size of the present series does not enable us to be certain that such is the case. At present, it would seem that deflexion of the head does not materially inhibit descent except when associated with large babies, and that it then does not particularly magnify the inhibition characteristic of the large-sized infant.

Occiput posterior descends as rapidly as occiput anterior, if the baby be of small and medium size. In the present series, occiput posterior averages for some rather large groups are actually less than occiput anterior averages. The large baby, however, with occiput posterior will show an average in excess of that of exactly comparable occiput anterior groups. The differential is four to eight minutes for primiparas, and zero to six minutes for multiparas. It would seem to us that occiput posterior, as a deterrent of descent, can be entirely neglected in the individual patient, as the effect is too inconstant for individual patient consideration.

If the membranes are ruptured previous to the completion of dilatation and the head still remains high until dilatation is complete, it was found by us that descent was more rapid in the second stage than if the membranes were still intact while descent was taking place in the second stage. The differential here is approximately four minutes with good pains and as much as eight minutes for exactly comparable groups whose pains are poor. Previous rupture of the membranes, therefore, facilitates descent. It is interesting, however, that all this advantage is lost after the head reaches the perineum, and the total time consumed by the

descent phase and the pelvic floor phase (combined) becomes exactly the same for those with early and those with late rupture of the membranes.

Failure of descent was observed only twice in this series. There was no instance of contracted pelvic inlet interfering with descent. One patient cared for during this period had a pelvis sufficiently small that elective cesarean section was done. Some five or six patients had sufficiently small pelvic outlets that there was delay in the pelvic floor phase. In no instance was this of serious degree. The obvious delay produced by abnormal presentations, such as bregma or brow, is not discussed here, as these abnormal presentations were not included in this study. Hydrocephalus occurring during this period happened to be associated with brow presentation in every case. There were observed one case of markedly delayed descent and one case of failure of descent. The marked delay was brought about by a huge amount of scar tissue in the pelvis following a previous ischiorectal abscess. The failure of descent was the result of the baby being suspended in a loop of its own umbilical cord. After many hours of failure of descent, a high median forceps delivery resulted in rupture of the cord followed by an extremely easy forceps extraction. Complete failure of descent is so rare in our experience that we have come to the rather firm conclusion that apparent failure of descent or apparent delay in descent is almost exclusively due to the fact that the cervix is not yet quite completely dilated. It is, therefore, a rule in our clinic that if the head is not on the pelvic floor within thirty minutes of the time dilatation was thought to be complete, a vaginal examination is to be done. This will nearly always reveal a rim of cervix still holding the head at a high station. The patient is, therefore, still in the first stage of labor, and the second stage has not begun.

Reference

1. Calkins, L. A.: *AM. J. OBST. & GYNEC.* 42: 802, 1941.

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Discussion

DR. HOWARD C. MOLOY, New York, N. Y.—The observations and conclusions of Dr. Calkins' paper confirm the general accepted opinion in regard to the importance of cervical dilatation and retraction, and the role played by the membranes in labor. Some years previously, we were interested in this subject at the Sloane Hospital and in a few instances studied cervical dilatation and retraction by the use of lateral roentgenograms after lead shot had been fixed to the anterior and posterior lip of the cervix. Until complete dilatation of the cervix had been obtained, the shot did not elevate. As the head descended through the completely dilated cervix, however, the cervix apparently rapidly retracted, either by passive force or by pulling through action of the uterine muscles proper. It was surprising to note that the cervical rim in normal labor can be retracted as high as the plane of the pelvic inlet.

The second point which interests me is not mentioned in the paper; namely, the possible role of pelvic size and shape. I think this factor is too important to be completely ignored in any report pertaining to the study of labor. Dr.

Calkins states that, "It was noted that if internal rotation took place during descent, that descent was completed on the average more rapidly than if internal rotation did not occur until the presenting part was definitely on the perineum." He suspects a factor exists to explain this observation by stating, "It may be that some factor which inhibits internal rotation during descent, also inhibits descent itself, as for example, the large size of baby," but does not refer to the possible influence of pelvic shape and size. We believe that pelvic shape plays a decided role in determining the level at which internal rotation takes place. Sometimes this is due to the shape of the inlet.

Torpin reported at the recent meeting of the American Medical Association in Chicago an interesting paper on the role played by the placenta upon head position. He studied roentgenologically pelvic shape in twelve cases of spontaneous face to pubis deliveries. In at least one-half of these cases he found marked anthropoid pelves or pelves with converging side walls to explain the failure of internal rotation. In the remainder, the presence of a large pelvis led him to suspect that the position of the placenta may have been a factor in the cause of this mechanism.

In five or six cases in Dr. Calkins' report there was definite delay in the pelvic floor stage or at the outlet. Although, in these cases, delivery was effected without difficulty, I feel certain that pelvic abnormalities in the outlet contributed to the delay or arrest. I would like Dr. Calkins to comment upon the possible influence of the bony pelvis in those cases of delayed internal rotation and those few cases which experienced difficulty during the pelvic floor phase.

The question of the significance of deflection attitudes of the head has for years entered into most discussions concerning the mechanism of labor. The fact that the anterior fontanel can be easily palpated is used as an argument that deflection exists, yet stereoscopic films may show that the head actually is quite well flexed in regards to the pelvis. While I agree in general with Dr. Calkins, therefore, that deflection does not play a significant part in the mechanism of labor, I would be interested in the clinical methods he used to determine this point.

The third and final point of interest deals with the remarkably low incidence of operative deliveries in this large series of cases. Failure of descent was observed only twice in the series and in only five or six cases was there delay at the outlet. I believe the excellent results indicate attention to the intrapartum care of the patient, the careful use of analgesia with adequate fluid intake in cases of protracted labor to prevent the uterus and the forces of labor from losing their efficiency.

It is doubtful, if it is entirely justifiable to compare the operative incidence from widely separated hospitals inasmuch as racial stock is a very important factor. The number of operative deliveries increases in mixed populations and, in large cities, racial types differ, and abnormal physical types, which predispose to soft part and bony dystocia are not infrequently encountered. All of these factors must be considered in the appraisal of obstetrical statistics.

DR. NORRIS W. VAUX, Philadelphia, Pa.—We all, I think, are in accord that in about 50 per cent of our patients who present no abnormalities of the birth canal or fetal obstruction, the presenting part reaches the pelvic floor at the completion of the first stage of labor. The other 50 per cent of patients, those in whom dilatation may occur before the descent phase is completed or those in which the presenting part is on the pelvic floor before the cervix is completely dilated, are the ones in which we are particularly interested.

It has always been our custom at the Lying-in Hospital to instruct the nursing staff that until the cervix is fully retracted or completely dilated not to allow the patient to use any of the accessory muscles for expulsion or aiding in the descent of the vertex. In all probability the use of the accessory muscles along

with the uterine contractions causes the cervix to lacerate and the membranes to rupture before the hydrostatic action of the unruptured sac upon the cervix is completed.

Rupturing of the membranes before complete dilatation is still a disputed and controversial subject. Leaving the membranes intact, if possible, until the cervix is fully dilated when Nature by virtue of the uterine contractions alone causes spontaneous rupture is, I believe, the best method to pursue. Although the labor might be somewhat delayed throughout the second stage, it is quite evident that the descent is more rapid after the rupture of the membranes if the cervix is fully dilated.

The management of the pelvic floor phase is no longer a matter for too serious consideration. With the recent advent of caudal analgesia the first stage of labor has become rapid and astounding in its completeness. The perineal floor is completely relaxed so that it is unnecessary to consider a delay in either the first stage of labor or the descent phase of the second stage of labor as the mechanism is completely changed at this time. This rapid dilatation of the cervix and descent of the presenting part under caudal analgesia is one of the outstanding points which occur when this method of analgesia is used. I am now confident that the accessory muscle force which previously was considered necessary in the bearing down action of a patient during the descent phase is no longer necessary or justifiable as the presenting part under caudal analgesia relaxation is placed promptly at the vaginal outlet and is frequently spontaneously delivered without any exertion on the patient's part. When this stage is reached, the patient can be promptly delivered, and should be, by the simple application of outlet forceps.

I am glad that Dr. Calkins has stressed the importance of the accurate diagnosis of position and station of the presenting part by vaginal examination, as well as the amount of dilatation and effacement of the cervix which exists. Too many rectal examinations, it seems, are done solely for the purpose of estimating the descent of the presenting part as it is not always possible by rectal examination to make an accurate diagnosis of the completely dilated and effaced cervix. A careful and well-executed vaginal examination is harmless and too frequent rectal examinations may produce more infection than one good vaginal examination.

I cannot subscribe to the conservative methods of delivery after the presenting part has reached the pelvic floor. Either manual or forceps rotation or decomposition and extraction of the breech can be very easily accomplished if the relaxation of the perineum exists as in a properly acting caudal analgesia.

Caudal analgesia will have to be given eventually its proper place in the conduct of labor, as it has been definitely conceded that dilatation of the cervix is more rapid and the descent phase is shortened considerably in both the multiparous and the primiparous patient.

PATHOLOGY OF MALIGNANT NEOPLASM OF THE CERVIX COINCIDENT WITH PREGNANCY*

CHARLES R. MAINO, M.D., ALBERT C. BRODERS, M.D., AND
ROBERT D. MUSSEY, M.D., ROCHESTER, MINN.

(From the Mayo Clinic)

IN A recent communication by two of us (Maino and Mussey)¹ a report was made of a study of twenty-five cases of carcinoma and one case of sarcoma of the cervix which complicated pregnancy. As an incidental finding pregnancy occurred in 0.7 per cent of the cases of malignancy of the cervix observed at the Mayo Clinic in nearly thirty-two years, that is, from July 1, 1909 to February 28, 1941. In this series of cases, many of which were observed before the present methods of treatment were developed, the prognosis appeared to be at least as favorable as the prognosis of carcinoma of the cervix which is not coincident with pregnancy.

Of the entire group of twenty-six patients, in twenty instances a follow-up period of at least five years had elapsed on February 28, 1941; of these twenty, six were alive and free of recurrence five or more years after the diagnosis was made, a "cure" rate of 30 per cent. On March 15, 1944, four more of the six remaining patients (21, 22, 23 and 24) had been followed at least five years; patients 21 and 22 were alive and free of recurrence, making a total of eight living patients out of twenty-four, a "cure" rate of 33 per cent.

The scope of the communication referred to in the previous paragraphs did not permit adequate description of the pathology of the disease. It is proposed in this paper to present in greater detail the pathology of malignant neoplasia of the cervix in cases in which the patients were also pregnant. The paper will include a résumé of the literature pertaining to the pathology of the disease, its symptoms as they relate to the type, stage and microscopic grade of the neoplasm, a study of the pathologic characteristics of the cases and consideration of the connection between these phases of the pathology and the prognosis. Symptoms, diagnosis, and treatment, and their bearing on the prognosis of carcinoma of the cervix coincident with pregnancy have been described previously. For the information of the reader, Table I of the former paper, with some additional data, is appended.

*Read by Dr. Mussey at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19, 20 and 21, 1944. Abridgment of a portion of thesis submitted by Dr. Maino to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M.S., in Surgery. Dr. Maino is now on active service in the Medical Corps of the United States Navy. The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

A large majority of malignant neoplasms of the cervix are squamous cell epitheliomas. Among the cases of forty-five authors who reported the microscopic examination of the fifty-nine cases of carcinoma of the cervix coincident with pregnancy, squamous cell epithelioma was present fifty times, adenocarcinoma seven times and the mixed cell type was observed twice.

Certainly squamous cell epithelioma predominates in reports of these cervical neoplasms. Bowing² stated that squamous cell epitheliomas comprise 90 per cent, adenocarcinoma 5 to 8 per cent and the remainder a combination of these two types of carcinoma; these figures include nonpregnant as well as pregnant patients.

Three cases of adenocarcinoma of the uterine corpus coincident with pregnancy have been reported by Schumann³ in 1927, Wallingford⁴ in 1934, and Westman⁵ in 1934.

The normal histologic changes in the cervix during pregnancy have been reported by Hofbauer,⁶ Levey⁷ and others. During pregnancy both the surface epithelium and glandular elements proliferate. The single layer of columnar cells with basal nuclei becomes stratified, that is, becomes several layers in thickness and the nuclei are then not usually found in the basal part of the cell. The glandular epithelium branches and permeates the stroma, forming a loose tissue almost like a spongiosa. Vacuoles or sinuses appear in the mucosa between the layers of columnar cells. The basal cells may show mitosis and the basement membranes may be indistinct. The resulting picture has been confused with that of malignant neoplasm. However, the cells are uniform and the basement membrane is intact; facts that should help distinguish the changes occurring in pregnancy from those of carcinoma.

Hofbauer⁶ mentioned a proliferation of subepithelial cells which may push up and even entirely replace the columnar epithelium. These new cells then resemble stratified squamous epithelium. Fluhmann⁸ earlier had commented on small basal cells or perhaps what may be cell rests which, by proliferation, raised the cylindrical epithelium and replaced it and then became differentiated into squamous epithelium. He termed this phenomenon epidermalization and warned that this benign tissue may be confused with cancer. His material, although obtained from nonpregnant women, seems to show a process similar to the changes described by Hofbauer in the pregnant cervix.

The cellular changes are at their height in the central and lower portion of the cervix at about the third month of gestation, while the upper portion undergoes these changes somewhat later.

Hyperplastic changes in the squamous epithelium of the vaginal portion of the cervix were described by Levey⁷ as paralleling those changes described for the columnar epithelium. Such hyperplastic changes in the squamous epithelium have been confused with low grade squamous cell carcinoma. The differential diagnosis is simplified, however, by the

TABLE I. MALIGNANT NEOPLASIA OF CERVIX COMPLICATING PREGNANCY: CLINICAL AND PATHOLOGIC FINDINGS

| CASE | YEAR OF OBSERVATION | AGE (YR.) | GRAVIDA | PARA | STAGE OF PREGNANCY | MALIGNANT LESION | | GRADE | DURATION OF SYMPTOMS | TREATMENT | RESULTS, INTERVAL AFTER TREATMENT | |
|------|---------------------|-----------|---------|------|--------------------|---|-------|-------|----------------------|--|-----------------------------------|---------|
| | | | | | | TYPE | STAGE | | | | ALIVE | DIED |
| 1 | 1909 | 33 | 5 | 3 | Term | No report | IV | | 4 mos. | Porro cesarean operation, subtotal hysterectomy | | 3 days |
| 2 | 1912 | 31 | 8 | 4 | Term | Squamous cell epithelioma | II | 4 | 5 mos. | Cesarean section; total abdominal hysterectomy | | 9 mos. |
| 3 | 1915 | 33 | 5 | 2 | 22 wks.* | Squamous cell epithelioma | II | 3 | 6 mos. | Total abdominal hysterectomy | 23 yrs. | |
| 4 | 1916 | 36 | 5 | 5 | Term | Squamous cell epithelioma; adenocarcinoma | II | 3 | Post partum 1 mo. | Vaginal hysterectomy | | 15 mos. |
| 5 | 1916 | 35 | 7 | 5 | 16 wks. | Squamous cell epithelioma | II | | 9 mos. | Radium and roentgen therapy | | 8 mos. |
| 6 | 1916 | 40 | 8 | 8 | Term | Squamous cell epithelioma | III | | 6 mos. | Radium and roentgen therapy | | 8 mos. |
| 7 | 1917 | 34 | 11 | 3 | 6 wks. | Squamous cell epithelioma | I | 4 | 7 mos. | Vaginal hysterectomy; radium and roentgen therapy | 12 yrs. | |
| 8 | 1918 | 35 | 2 | 1 | 18 wks. | Squamous cell epithelioma | IV† | 3 | 2 yrs. | Hysterectomy elsewhere; radium and roentgen therapy here | | 6 yrs. |
| 9 | 1919 | 37 | 11 | 11 | Term | | III | | 2 mos. | Porro's cesarean operation; radium therapy | | 4 mos. |
| 10 | 1919 | 28 | 7 | 5 | 12 wks. | Squamous cell epithelioma | II | 4 | 5 mos. | Total abdominal hysterectomy; radium therapy | | 4 mos. |

*Through error period of gestation was stated as thirty weeks in previous paper.

†Operation by local physician; Stage IV here two years later.

‡Operation performed two months after vaginal delivery.

§This paper deals prevalently with carcinomas; this one case of myxosarcoma was not excluded from the series. Panhysterectomy was performed.

‡March, 1914.

| | | | | | | | | | | | |
|----|------|----|----|----|---------|------------------------------|-----|---|---------|--|---------|
| 11 | 1919 | 26 | 5 | 4 | Term | Squamous cell epithelioma | I | 4 | 1 yr. | Vaginal hysterectomy; radium and roentgen therapy† | 2 yrs. |
| 12 | 1920 | 29 | 5 | 4 | 32 wks. | Squamous cell epithelioma | IV | 3 | 4 mos. | Cesarean section; subtotal hys- terectomy; radium and roent- gen therapy | 1 wk. |
| 13 | 1922 | 28 | 4 | 3 | 25 wks. | Myxosarcoma | I | 3 | 1 yr. | Panhysterectomy | 1 yr. |
| 14 | 1928 | 32 | 2 | 1 | 10 wks. | Squamous cell epithelioma | III | 3 | 6 mos. | Radium and roentgen therapy | 11 yrs. |
| 15 | 1928 | 39 | 13 | 11 | 6 wks. | Adenocarcinoma | II | 2 | 1 yr. | Total abdominal hysterectomy; radium and roentgen therapy | 10 yrs. |
| 16 | 1928 | 27 | 5 | 4 | 18 wks. | Squamous cell epithelioma | II | 4 | 2 mos. | Total abdominal hysterectomy; radium and roentgen therapy | 11 yrs. |
| 17 | 1928 | 34 | 7 | 2 | 16 wks. | Squamous cell epithelioma | I | 4 | 6 mos. | Total abdominal hysterectomy; radium and roentgen therapy | 11 yrs. |
| 18 | 1932 | 27 | 2 | 1 | Term | Squamous cell epithelioma | IV | 3 | 2 mos. | Radium therapy | 5 mos. |
| 19 | 1932 | 32 | 2 | 2 | Term | Squamous cell epithelioma | III | 3 | 9 mos. | Radium and roentgen therapy | 10 mos. |
| 20 | 1934 | 28 | 3 | 2 | 20 wks. | Squamous cell epithelioma | III | 4 | 1 yr. | Hysterotomy; radium and roentgen therapy | 22 mos. |
| 21 | 1936 | 35 | 1 | 0 | 8 wks. | Adenocarcinoma | I | 2 | 0 | Total abdominal hysterectomy; radium and roentgen therapy | 8 yrs. |
| 22 | 1937 | 34 | 7 | 3 | 27 wks. | Adenocarcinoma | I | 1 | 1½ yrs. | Wertheim's operation (1939); radium and roentgen therapy | 5 yrs. |
| 23 | 1939 | 26 | 3 | 1 | 15 wks. | Squamous cell epithelioma | III | 3 | 6 mos. | Radium and roentgen therapy | 17 mos. |
| 24 | 1939 | 31 | 2 | 2 | Term | Squamous cell epithelioma | II | 3 | 14 mos. | Porro's cesarean operation else- where; radium and roentgen therapy | 14 mos. |
| 25 | 1940 | 25 | 3 | 2 | 10 wks. | Squamous cell epithelioma | II | 4 | 3 mos. | Wertheim's operation; radium and roentgen therapy | 4 yrs. |
| 26 | 1941 | 41 | 9 | 6 | 14 wks. | Squamous cell epithelioma | I | 4 | 1 yr. | Wertheim's operation; radium and roentgen therapy | 3 yrs. |

statement of one of us (Broders⁹) that he has not observed a case of grade 1 squamous cell epithelioma of the cervix.

Various authors have reported decidual reaction in 25 to 50 per cent of cases of pregnancy. According to Levey this incidence may be too high since swollen stromal cells easily may be confused with true decidual cells. Stöckl¹⁰ credited the decidua with a marked resistance to invasion by cancer. He stated that this explains the extreme rarity of invasion of fetal membranes or the fetus by the carcinoma.

In reporting a case of sarcoma of the uterus complicating pregnancy, in 1930, Hesseltine¹¹ mentioned the case reports of six others in the literature. DerBrucke,¹² three years later, apparently not familiar with Hesseltine's article, found only three cases previously reported. All this literature deals with sarcoma of the myometrium or of fibromyomas, except for one case reputed to have been of endometrial origin. There was no case of primary sarcoma of the cervix.

It seems pertinent to speak of symptoms as these relate to the stage and microscopic grade of carcinoma. Bleeding was the most common symptom of the disease, as there was abnormal bleeding in all but three cases; it was the primary symptom in nearly 90 per cent of the cases. Later, odorous, watery discharge was a common symptom. It is not surprising to find that there was a significant difference in the duration of symptoms up to the time of diagnosis, between the cases in Stage I and those in Stage IV of the disease. However, there is no significant predominance of grade 4 lesions among the further advanced cases (Table II).

Data in Table II regarding the stage or extent of the lesion, the duration of symptoms and the stage of pregnancy are of interest. These data show that the duration of symptoms of cases in which the lesions were of Stage II or III averaged approximately six months prior to the institution of treatment, the symptoms of cases in which the lesions were of Stage I averaged nine months, and the symptoms of cases in Stage IV averaged approximately three months. If the neoplasm can attain Stage IV in a third of the time that it may exist as a Stage I lesion, then one would expect to find the more rapidly growing high grade carcinoma to occur in the Stage IV group, but when the grade of the neoplasm is checked for various stages, there is no definite tendency for grade 4 lesions to occur in the more advanced stages. This may be explained, perhaps, by the restraining influence on cancer of the cervix attributed to pregnancy by some writers.

Among the six cases in which the lesions were of Stage I, four of the fetuses were previsible, one was decidedly premature and one gestation (17 per cent) was at term.

Of the Stage II group, three (33 per cent) of the nine had arrived at term, one was aborted therapeutically prior to irradiation, in one case there was spontaneous abortion and in the remainder (four) pregnancy was terminated early by hysterectomy. Among Stage III lesions,

TABLE II. STAGES OF CARCINOMA OF THE CERVIX

| CASE | DURATION OF SYMPTOMS | | TYPE AND GRADE | STAGE OF PREG-NANCY, WEEKS | PREGNANCY TERMINATED BY | |
|---------------------|----------------------|------------------|---------------------------|----------------------------|-------------------------|--|
| | MONTHS | AVERAGE MONTHS | | | | |
| Stage I | | | | | | |
| 21* | 0 | 9.2 | Adenocarcinoma | 2 | 8 | Hysterectomy |
| 22* | 18 | | Adenocarcinoma | 1 | 27 | Hysterectomy |
| 17† | 6 | | Squamous cell epithelioma | 4 | 16 | Hysterectomy |
| 7† | 7 | | Squamous cell epithelioma | 4 | 6 | Vaginal hysterectomy |
| 11 | 12 | | Squamous cell epithelioma | 4 | Term | Vaginal delivery |
| 26 | 12 | | Squamous cell epithelioma | 4 | 14 | Hysterectomy |
| Stage II | | | | | | |
| 4 | 1† | 6.3 | Squamous cell epithelioma | 3 | Term | Vaginal delivery |
| | | | Adenocarcinoma | | | |
| 16† | 2 | | Squamous cell epithelioma | 4 | 18 | Hysterectomy |
| 25 | 3 | | Squamous cell epithelioma | 4 | 10 | Hysterectomy |
| 2 | 5 | | Squamous cell epithelioma | 4 | Term | Cesarean section |
| 10 | 5 | | Squamous cell epithelioma | 4 | 12 | Hysterectomy |
| 3† | 6 | | Squamous cell epithelioma | 3 | 22 | Hysterectomy |
| 5 | 9 | | Squamous cell epithelioma | — | 16 | Therapeutic abortion |
| 15† | 12 | | Adenocarcinoma | 2 | 6 | Spontaneous abortion |
| 24 | 14 | | Squamous cell epithelioma | 3 | Term | Porro's cesarean operation |
| Stage III | | | | | | |
| 9 | 2 | 6.8 | No report | | Term | Porro's cesarean operation |
| 6 | 6 | | Squamous cell epithelioma | — | Term | Vaginal delivery |
| 14† | 6 | | Squamous cell epithelioma | 3 | 10 | Abortion after irradiation |
| 23 | 6 | | Squamous cell epithelioma | 3 | 15 | Abortion after irradiation |
| 19 | 9 | | Squamous cell epithelioma | 3 | Term | Vaginal delivery |
| 20 | 12 | | Squamous cell epithelioma | 4 | 20 | Hysterotomy |
| | | | | | | |
| | | | | | | |
| Stage IV | | | | | | |
| 18 | 2 | 3.3 | Squamous cell epithelioma | 3 | Term | Vaginal delivery |
| 1 | 4 | | No report | | Term | Porro's cesarean operation |
| 12 | 4 | | Squamous cell epithelioma | 3 | 32 | Cesarean |
| Miscellaneous Cases | | | | | | |
| 8 | 24 | Stage not known‡ | Squamous cell epithelioma | 3 | 18 | Operation by local physician; stage 4 here 2 years later |
| 13 | 12 | Stage I | Myxosarcoma | 3 | 25 | Operation |

*Living five or more years.

†Living ten or more years.

‡Post partum.

§Stage IV when seen here; about Stage II when seen by local physician; rapid progression.

the proportion of term to previable pregnancies increases to three and three respectively (50 per cent). Stage IV is seen to include only patients who were in far advanced pregnancy. Of the three patients, two (67 per cent) were at term and one had a gestation of seven and a half months.

The patient of Case 24, when seen at the clinic, was in Stage IV of the disease, although she was but two months post partum. She had been delivered at term by Porro-cesarean section and was believed to be in Stage II at that time. One month later, in spite of radium treatment, there was a metastatic mass in the right adnexa. This case would seem to agree with the cases in Stage IV cancer, in which the progress of the disease was very rapid and all associated with term or near term deliveries. Though the patient's symptoms are given as of fourteen months' duration in the table, a word of explanation is in order. In January, 1938, she had noted a little watery discharge on a few occasions but it did not persist. In the spring of 1938, she noticed spotting. In July of 1938, she became pregnant. During this time her only symptom was a little watery discharge at the time her menses should have occurred. On October 23, there was slight bleeding. She was examined on October 25, by a responsible physician and the cervix was clean at that time. Six months later, she was delivered at term, and was found to have a well-advanced carcinoma of the cervix.

Another patient (Case 13) had had odorous discharge and metrorrhagia for at least one year before a myxosarcoma was diagnosed. At the onset of her symptoms a year previously, she had been in the eighth month of gestation and had been told that she had cervical polyps. A few weeks after delivery these "growths" projected from the vagina. The polyps were excised once six months after the onset of the symptoms and again six months later, at which time she was again pregnant. It seems probable that the original polyps noted at the eighth month of gestation one year previous to her registration at the clinic were myxosarcoma. Certainly, when she was seen at the clinic, at which time she was in approximately the twenty-fifth week of gestation, she had large myxosarcomatous polyps which protruded from the vagina. This was only two months after the second excision of polyps which had protruded from the vagina.

Pathologic Study

A microscopic examination of tissue was made in twenty-four of the twenty-six cases, and the diagnosis of malignant neoplasm was confirmed.

Sections of tissue were available for review in twenty-two of the twenty-six cases. Two specimens (5 and 6) had dried in the course of their storage, which had been since 1916. This tissue was therefore, rendered unfit for pathologic examination. However, in both these cases, the tissue had originally been examined by Dr. W. C. MacCarty and a report of epithelioma had been made. There were no microscopic pathologic reports on Cases 1 and 9, nor was there tissue available to supply this deficiency. These last two mentioned are included in the series, however, because the clinical history and course of the disease were typical of cancer of the cervix, an unqualified diagnosis of cancer of the cervix was made by both the surgeon and the clinician and an adequate description of the lesions was given in both cases. To quote from the records, the patient in Case 1, seen in 1909, was said to have a "hard nodular carcinoma of the cervix" and the patient in Case 9, seen in 1919, had a "large fungating cancer of the cervix with hemorrhage and hard nodules palpable by rectum."

Table III shows the relation of the size of the lesion to other data. Seven patients in the group studied had lesions of medium size; that is, 2 to 4 cm. in diameter. Eighteen had large lesions of 4 cm., or more. Small lesions, less than 2 cm. in diameter, were not encountered. In Case 8 the stage and size of the lesion at time of original treatment are not known.

The proportion of medium-sized lesions is apparently not modified by a coexisting pregnancy. Among the pregnant women, 28 per cent had lesions of medium size. This figure agrees very closely with the 27.12 per cent of medium-sized lesions which one of us (Broders) found in nonpregnant women who had cervical cancer. In his study, he found that 6.47 per cent had small lesions and 66.39 per cent had large lesions. Since no small lesions were found among the pregnant group, the percentage of large lesions is therefore relatively higher (72 per cent) than in the nonpregnant group. Theoretically, one or two patients in the pregnant group should have small cervical cancers, but the number in this group is small, and a variation from the theoretical distribution is to be expected. Therefore, it would seem unwise to make any conclusions relative to the activity of the cancer due to pregnancy because such results would be without statistical significance.

In nineteen of the twenty-six neoplasms the type was known to be squamous cell epithelioma. Seventeen of the epitheliomas were graded; nine (53 per cent) were grade 4, and eight (47 per cent) were grade 3. In the series of one of us (Broders), only 34.5 per cent were grade 4 squamous cell epithelioma while 56.87 per cent were grade 3, and 8.54 per cent were grade 2. There appears to be a disproportion of high grade tumors of squamous cell epithelioma type among those who were pregnant.

Mixed adenocarcinoma and squamous cell epithelioma, grade 3, occurred once; there were two grade 2 adenocarcinomas, and one grade 1 adenocarcinoma. A case of myxosarcoma, grade 3, was also included. In two cases no tissue was available for microscopic examination.

The relation between the grade of the lesion and the extent of the cancer in this group is not outstanding. Among the medium-sized lesions there was one grade 2 adenocarcinoma, two (29 per cent) grade 3 squamous cell epitheliomas, two (33 per cent) grade 4 squamous cell epitheliomas, and one mixed grade 3 adenocarcinoma and squamous cell epithelioma. One medium-sized squamous cell epithelioma was not graded. A rather comparable distribution was found among the large-sized carcinomatous lesions; seven (50 per cent) were grade 4 squamous cell epitheliomas, five (36 per cent) grade 3 squamous cell epitheliomas and one each of grade 1 and grade 2 adenocarcinoma, and one grade 3 myxosarcoma. There were also one large ungraded squamous cell epithelioma and two large malignant lesions for which neither the type nor the grade was recorded. Similarly, there was no relation between the extent or stage of the disease and the grade of the lesion.

TABLE III. RELATION OF SIZE OF LESION TO OTHER DATA *

| CASE | INTERVAL TO LAST REPORT | | TIMES- TER OF PREG- NANCY | TYPE | SIZE | GRADE | TREATMENT |
|-----------|----------------------------|---------|------------------------------------|---------------------------|------|-------|--|
| | LIVING | DEAD | | | | | |
| Stage I | | | | | | | |
| 7 | 12 yrs. | 2 yrs. | First Term | Squamous cell epithelioma | L† | 4 | Vaginal hysterectomy; radium and roentgen therapy |
| 11 | | 1 yr. | Second | Squamous cell epithelioma | M† | 4 | Vaginal hysterectomy; radium and roentgen therapy |
| 13 | | | Second | Myxosarcoma | L | 3 | Total abdominal hysterectomy; radium and roentgen therapy |
| 17 | 11 yrs. | | Second | Squamous cell epithelioma | L | 4 | Total abdominal hysterectomy; radium and roentgen therapy |
| 21§ | 8 yrs. | | First | Adenocarcinoma | M | 2 | Total abdominal hysterectomy; radium and roentgen therapy |
| 22§ | 5 yrs. | | Second | Adenocarcinoma | L | 1 | Total abdominal hysterectomy (Wertheim); radium and roentgen therapy |
| 26 | 3 yrs. | | Second | Squamous cell epithelioma | L | 4 | Wertheim's total abdominal hysterectomy; radium and roentgen therapy |
| Stage II | | | | | | | |
| 2 | 23 yrs. | 9 mos. | Term | Squamous cell epithelioma | L | 4 | Cesarean section; total abdominal hysterectomy |
| 3 | | 15 mos. | Second Term | Squamous cell epithelioma | L | 3 | Total abdominal hysterectomy |
| 4 | | | Term | Squamous cell epithelioma | M | 3 | Vaginal hysterectomy |
| 5 | | 8 mos. | Second | Adenocarcinoma | M | - | Exploration; radium and roentgen therapy |
| 10 | | 4 mos. | First | Squamous cell epithelioma | L | 4 | Total abdominal hysterectomy; radium therapy |
| 15 | 10 yrs. | | First | Squamous cell epithelioma | L | 2 | Total abdominal hysterectomy; radium and roentgen therapy |
| 16 | 11 yrs. | | Second | Adenocarcinoma | L | 4 | Total abdominal hysterectomy; radium and roentgen therapy |
| 24§ | | 14 mos. | Term | Squamous cell epithelioma | M | 3 | Porro's cesarean operation; radium and roentgen therapy |
| 25 | 4 yrs. | | First | Squamous cell epithelioma | L | 4 | Wertheim's operation; radium and roentgen therapy |
| Stage III | | | | | | | |
| 6 | | 8 mos. | Term | Squamous cell epithelioma | L | - | Radium and roentgen therapy |
| 9 | | 4 mos. | Term | Squamous cell epithelioma | L | - | Porro's cesarean operation; radium therapy |
| 14 | 11 yrs. | | First | Squamous cell epithelioma | M | 3 | Radium and roentgen therapy |
| 19 | | 10 mos. | Term | Squamous cell epithelioma | L | 3 | Radium and roentgen therapy |
| 20 | | 22 mos. | Second | Squamous cell epithelioma | M | 4 | Hysterotomy; radium and roentgen therapy |
| 23§ | | 17 mo. | Second | Squamous cell epithelioma | L | 3 | Radium and roentgen therapy |
| Stage IV | | | | | | | |
| 1 | | 3 days | Term | Squamous cell epithelioma | L | - | Porro's cesarean operation and subtotal hysterectomy |
| 12 | | 1 wk. | Third | Squamous cell epithelioma | L | 3 | Porro's cesarean operation; subtotal hysterectomy; radium and roentgen therapy |
| 18 | | 5 mos. | Term | Squamous cell epithelioma | L | 3 | Radium therapy |

*Case 8 not included. Stage at time of first treatment unknown.

†L = Large-sized lesion (diameter over 4 cm.).

‡M = Medium-sized lesion (diameter 2 to 4 cm.).

§Report March, 1944.

One may note, however, that there are only two in six (33 per cent) of the medium-sized lesions in which the cancer was graded as 4, while in the large-sized lesions, seven in fifteen (46 per cent) were graded 4. This would suggest a relatively faster progression of the grade 4 cancer. However, in review, both grade 4 lesions of medium size had evidenced symptoms for one year, a longer period of time than the average regardless of the type of growth. A grade 4 cancer could have been expected to produce a large lesion during the course of a year.

The average duration of symptoms of large lesions caused by grade 4 cancer was 4.1 months, while a slightly shorter duration (3.6 months) was discovered in the case of grade 3 cancer.

Medium-sized lesions, whether of grade 3 or 4, gave symptoms on the average of ten months. The longer duration of symptoms coupled with a relatively smaller lesion suggests some restraining influence on the rate of tumor growth in these selected instances.

Apparently, it is not the grade alone, nor the duration of symptoms alone, that determines the rate of growth or whether a lesion shall be of large or moderate size when it is discovered.

A few words are necessary to explain Case 22. In this case, a grade 1 lesion had produced a large growth and the woman had no symptoms referable to cervical cancer at the time the tumor was discovered. It was not until one and one-half years after the malignant lesion was recognized and microscopically verified that she submitted to radical operation. The slow growth here is compatible with the low grade of malignancy. The fact that two pregnancies had supervened on the cancer does not appear to have accelerated the growth.

Two of seven patients who had moderate-sized lesions were living when the last report was received. These two have been followed more than five years; one was free of recurrence after five, and one after eleven years. A third patient, Case 11, who was apparently free of disease in her second year met accidental death. If this case is omitted, the per cent of probable cures is two in six, or 33 per cent.

Eighteen patients had large lesions, and of these, eight were living at the last report. Sixteen of these patients have been followed five years or more, and of these six, or 37.5 per cent, are living and apparently free of recurrence. Five of these patients have all lived ten years or more (twenty-three, twelve, eleven, eleven and ten years), and one has lived more than five years.

In the study by one of us (Broders) on nonpregnant women which will serve as a control, only 10 per cent of patients who had large lesions, and 33 per cent of those who had medium-sized lesions obtained good results. Among the group as a whole, 19.8 per cent were considered to have obtained a good result. Twenty-four patients in the pregnancy group have been followed five or more years, and eight (33 per cent) were free of recurrences for an average of more than

ten years. This comparison would indicate that pregnant women who had cervical carcinoma fared significantly better than those in the nonpregnant group.

It is perhaps well to mention here again the possibility of confusing a malignant lesion with the hyperplastic changes in the cervix of a pregnant woman. Clinically, the pregnant cervix may on occasion appear sufficiently abnormal to cause the examiner to suspect that a malignant lesion is present. The cervix may be coarsely granular, and the small firm excrescence may bleed on slight trauma.

Biopsy will prove the nature of the suspected tissue. A qualified pathologist should not have any difficulty in recognizing the normal pregnancy reactions of the cervix as a benign tissue phenomenon. The cells are uniform and regular and growth is orderly. Mitoses may occasionally be observed in the basal cells but pathologic mitoses are absent. The staining characteristics are typically benign. This picture is in marked contrast to that of malignancy.

One in six (17 per cent) of Stage I patients (not counting the patient who had myxosarcoma) was at term at the time the diagnosis was made. Three in nine (33 per cent) were at term with Stage II, three in six (50 per cent) at term with Stage III cancer, and two in three (67 per cent) were at term with Stage IV. It would appear from this small group that advanced pregnancy is most likely to be associated with advanced carcinoma and that the prognosis is very poor when the patient is found to be at term.

Prognosis: Effect of Type and Grade of Cancer

Five of the six patients who lived ten or more years had squamous cell epithelioma; one (Case 15) had adenocarcinoma grade 2. Two who have lived eight and five years, respectively, had adenocarcinoma grades 1 and 2, respectively. Three of the twenty-four patients who have been observed for five years or more, were found to have adenocarcinoma, and all three were living and well at the last report.

All three adenocarcinomas were in the early stage of the disease when seen, two in Stage I, and one in Stage II, although in Case 22 symptoms and diagnosis of cancer had been recognized for one and a half years before treatment, and in Case 15 symptoms were in evidence for more than a year. The relatively slow progress of the disease in the cases of adenocarcinoma is probably due to their low grades of malignancy, rather than to the fact that they were of the adenocarcinoma type.

In Case 4, the lesion was a mixed adenocarcinoma and squamous cell epithelioma, grade 3. The patient had a total vaginal hysterectomy five weeks post partum, and died fifteen months later.

In the group of seventeen cases of squamous cell epithelioma of known grade, all of the lesions were of a high grade of malignancy, grades 3 and 4, and one would, therefore, expect a relatively poor

CARCINOMA CERVIX—PREGNANCY

| HOSPITAL | AGE | PREGNANT | TYPE | STAGE | GRADE | DURATION OF SYMPTOMS | TREATMENT | DURATION OF LIFE |
|----------------------|-----|----------|---------------|-------|--------------|----------------------|--|--|
| Woman's Temple | 39 | 5 mo. | Squamous cell | III | ? | 4 mo. | Radium 4,000 mc. hr. | Living and well 13 mo. |
| | 39 | 5 mo. | Squamous cell | II | 2 | 4½ mo. | High voltage therapy started | Living and well 2 mo. |
| | 32 | 3½ mo. | Squamous cell | Polyp | 1 | 2 yr. | Radium 3,000 mc. hr. | Living and well 3 yr. |
| | 29 | 6 mo. | Squamous cell | II | ? | 4 mo. | Cantery; amputation, radium 4,400 mc. hr. | 15 yr. (died of pneumonia) |
| University | 29 | 2 mo. | Squamous cell | I | Transitional | 3 wk. | Supravaginal hysterectomy Bilateral salpingo-oophorectomy Radium 2,400 mc. hr. | Living and well 18 yr. |
| | 38 | Term | Squamous cell | II | ? | 0 | High voltage therapy Radium 4,500 mc. hr. Total hysterectomy | Living and well 5 yr., 5 mo. |
| Philadelphia General | 31 | 2 mo. | Squamous cell | III | 4 | 1 mo. | Radium 3,600 mc.hr., intra-uterine Radium 6,600 mc.hr., intra-vaginal | Died 2 yr., 3 mo. (from metastasis to the liver) |

Five-year salvage seventy-five per cent. Seventy-one per cent lesions were in Stages I and II. Irradiation therapy used in every instance.

prognosis. It should be borne in mind, however, that among the non-gravid patients who have squamous cell epithelioma, 91.44 per cent have malignancy of grades 3 and 4.

Of the five patients suffering from squamous cell epithelioma who survived ten or more years, three had grade 4 lesions, and two had grade 3 lesions. These figures are too small to be of any statistical significance in an attempt to estimate prognosis differences between grades 3 and 4, since nine of the seventeen patients suffering from squamous cell epithelioma whose lesions were graded had grade 4, and eight had grade 3.

The one patient who had myxosarcoma met the fate common to patients suffering from this type of cervical malignant lesion. McDonald¹³ has shown that these tumors uniformly carry an extremely high mortality rate.

Prognosis by Stage of Cancer

Of six patients having Stage I carcinoma of the cervix, five were still living at the last report. One of these, however (Case 26), has been followed less than five years. The other four have been living twelve, eleven, eight and five years, respectively. The woman previously mentioned (Case 11) whose death was accidental, belongs to the Stage I group; she was apparently free of recurrence of cancer at the time of death. Thus, it is seen that in no instance in the group of six patients treated for Stage I squamous cell epithelioma or adenocarcinoma was death due to extension of the cancer. Including Case 11, the five-year cure rate of these cases of Stage I carcinoma of the cervix is 66 per cent.

In nine cases, the disease was given as Stage II. Four of the nine patients were living when the last communication was received. Eight have been followed five or more years, and of this number three were alive and well. This shows a "cure" rate of 38 per cent.

Six patients were determined to be in Stage III of their disease. Only one is known to be alive, and she is free of recurrence now in her eleventh year, a "cure" rate of 17 per cent.

As might be expected, all patients suffering from Stage IV cancer died from the disease or complications incident thereto. Two died in the postoperative period, and one because of advancing carcinoma.

Comment

The twenty-six cases studied represented 0.7 per cent of 3,570 cases of malignant neoplasm in which the patients were admitted to the clinic between 1909 and 1941. During this period, 8,500 pregnant women were given obstetric care but, since all of those whose pregnancy was complicated by cancer sought treatment primarily for the malignant condition rather than for obstetric care, the incidence of malignant lesions in this group of pregnant women cannot be estimated.

Of the entire group of twenty-six patients, in twenty-four instances a follow-up period of at least five years had elapsed in March, 1944; of these twenty-four, eight were alive and free of recurrence five or more years after the diagnosis was made, a "cure" incidence of 33 per cent.

Twenty-five of the twenty-six patients had carcinoma of the cervix and one patient had myxosarcoma. Of the twenty-five cases of carcinoma, there were nineteen cases of squamous cell epithelioma, three cases of adenocarcinoma, one case of mixed squamous cell epithelioma and adenocarcinoma, and two cases in which the type of carcinoma was not determined.

Bleeding was the primary symptom in nearly 90 per cent of the cases. Among patients in Stage I of the disease, the average duration of symptoms was nine months, as compared with three months for those in Stage IV. Grade 4 lesions were not more frequent in the more advanced cases than in the less advanced cases.

The extent or stage of the lesion corresponded in general to the duration or stage of pregnancy. Seventeen per cent of patients who had Stage I carcinoma, 33 per cent of those in Stage II, 50 per cent of those in Stage III, and 67 per cent of those in Stage IV had full-term pregnancies. Five of eight patients who lived five or more years had squamous cell epithelioma; three had adenocarcinoma. Of patients observed for five or more years, four of six patients who had Stage I carcinoma (66 per cent), three of eight patients in Stage II (38 per cent), one patient in Stage III (17 per cent), and no patients in Stage IV were alive five or more years after the malignant neoplasm of the cervix coincident with pregnancy was diagnosed.

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Discussion

DR. CHARLES A. BEHNEY, PHILADELPHIA, PA.—It is unfortunate, that in considering a subject like carcinoma of the cervix when one breaks down his series, the resultant groups are so small that it is difficult to draw any certain conclusions from the statistics. In reading Dr. Mussey's paper, I was impressed by the large total number of patients in which cancer of the cervix was complicated by pregnancy in a single institution and by the five-year salvage rate.

Through the courtesy of Dr. Margaret Sturgis of the Woman's Medical College, Dr. Thaddeus Montgomery of Temple University Medical School, Dr. Franklin L.

Payne of the University of Pennsylvania School of Medicine and Dr. Lewis C. Scheffey of Jefferson Medical College, I was able to collect 7 cases in which carcinoma of the cervix was complicated by pregnancy. In none of these institutions, including the Philadelphia General Hospital, is there any record of pregnancy complicated by sarcoma of the cervix. The material obtained from these various sources is represented in the following table, in a manner somewhat similar to Table I shown by Dr. Mussey.

In analyzing our statistics, I was surprised to find that in some of our Philadelphia institutions the complication of carcinoma of the cervix and pregnancy occurred almost as frequently as at the Mayo Clinic. For example, the incidence at Temple University is 0.7 per cent; at the University Hospital, 0.6 per cent; at the Woman's Medical College Hospital, 0.4 per cent; and at Philadelphia General Hospital, where it occurred in only two out of 1,751 cases of carcinoma of the cervix, 0.1 per cent.

The first three patients are living, less than five years after treatment. The fourth, fifth and sixth have survived for five or more years, the fourth having died of pneumonia, without evidence of recurrence of carcinoma 15 years after treatment. The last patient died two and a quarter years after treatment. Autopsy revealed liver metastases. Three of the latter 4 patients survived for five or more years, a salvage rate of 75 per cent. Every five-year survivor was treated with irradiation.

Whereas Dr. Mussey's series contains an unusually great number of adenocarcinomas, those from Philadelphia consist exclusively of squamous cell carcinomas. Unfortunately, some of our local pathologists for one reason or another, are reluctant to grade carcinoma, so that only three of our seven specimens were classified according to Broder's method. One of these was grade 4.

In evaluating statistics pertaining to the end results secured from the treatment of carcinoma, one should consider the proportion of early cases. In the Mayo group of patients, there were 60 per cent of cases in Stages I and II. The five-year salvage rate was 33 per cent. When I found that in the Philadelphia series 75 per cent of patients were living and well, five years after treatment, I was not surprised to discover that 71 per cent of these patients were in Stages I and II.

Another group of carcinoma of the cervix cases containing a large proportion of early lesions is the series from the Woman's Medical College Hospital in Philadelphia, reported by Dr. Catharine Macfarlane. I believe that as the result of Dr. Macfarlane's propaganda, her disciples and referring physicians are exceptionally alert in respect to pelvic examinations in general, and periodic examinations in particular, and that they recognize and refer to the Woman's Medical College Hospital a greater proportion of early cases than are sent to the average clinic. Obstetric patients are usually examined several times during the course of pregnancy, and it is understandable that at these periodic examinations during pregnancy, malignant lesions of the cervix are recognized before they reach an advanced stage.

One must be cautious about drawing any startling conclusions from statistics no larger than those provided by either or both of these groups. They may indicate, however, that the comparatively frequent pelvic examinations incident to proper prenatal care will disclose malignant disease of the cervix at an earlier stage than when the patient herself is left to consult a doctor after symptoms have developed. Early lesions give a high percentage of five-year cures, whether treated radiologically, surgically or by a combination of the two methods.

DR. CURTIS F. BURNAM, BALTIMORE, MD.—At The Kelly Clinic we have seen in 18 years, 13 cancers of the cervix in which pregnancy was a complication. There were 8 white women and 5 Negroes. The average age was 34 years. With one exception, they were all multipara. They were all treated by irradiation.

In three of these cases, the irradiation was given after the birth of the child. One of these three had a Porro-cesarean section, one an ordinary cesarean section, and the third a spontaneous delivery. Although bleeding had long been present in each case, none was recognized as cancer until after delivery. When first seen for the malignancy, all had bleeding and pain, and were very advanced. The children all survived; all three mothers died of cancer.

Of the remaining ten cases, one was at 2½ months, and the remaining nine between 4 months and full term. The two and a half months' patient was treated by therapeutic abortion and radiation, but the extent of the disease was too advanced to be controlled by treatment.

The remaining nine cases were treated by radiation and cesarean section when the child was viable. Of these nine cases, two were in advanced stages, one with parametrial fixation, the other with extensive vaginal involvement. Although apparently clear of cancer at the time of cesarean section, both of these mothers died of cancer—one after two years, and the other after five years.

Of the remaining seven cases, which were operable and early, five are living and free from cancer in periods from 6 to 18 years, one died of cancer after 2 years, and one is living but with an incurable cancer. This represents a five-year cure rate of 71 per cent.

As to the offspring, ten living children were obtained from nine mothers. Eight of them were normal children and two microcephalics. The microcephalics were in patients radiated at a four months' stage of pregnancy, while the normal children came from pregnancies that were further along when radiation was given. The extra child came from a mother who was treated for a very early cancer of the cervix with half the ordinary dosage. She was not sterilized at the cesarean section and a year later, came in four months pregnant, with a much more advanced cancer. This last child had severe developmental defects and died within a year, but the mother remains well after six years.

As to the histology, all were epidermoid cancers. One was classified as grade 2, one as grade 4, and eleven as grade 3. Tissue was obtained by punch biopsy in each case.

Among the five patients apparently well, three had had bleeding for about one month, one for three months, and one for five months before treatment. Among the five patients who died, one had had bleeding for less than a month, and four for more than three months.

With such a small series of cases, statistics mean little or nothing. The quip that there are two kinds of lies—white lies and statistics—is worth remembering. In going over the results of treatment of operable cancers of the cervix, when we were treating about twenty such cases a year, we found variations in five-year cure rates which in two contiguous years varied from 100 per cent to 30 per cent. The methods of examination, classification and treatment were essentially identical in these years.

Involving two lives, with various economic, family and personal angles, it is difficult to lay down hard and fast rules of procedure for the treatment of cancer of the cervix in pregnancy. Three groups may, however, be recognized.

Group One.—*Patient pregnant more than four months with disease limited to the cervix.* Here, radium should be used and when the child is viable a cesarean section performed. If at the time of operation everything is clear, after careful examination, approximate x-ray therapy should be given as soon as the incision is healed. If anything suggestive of disease is found and it is feasible, appropriate surgery should be performed followed by radiation with x-ray.

Group Two.—*Patients observed with cancer of the cervix and with pregnancies less than four months.* The hope of saving both the child and the mother should be abandoned, and treatment carried out as in a nonpregnant woman with similar involvement by the cancer.

Group Three.—*Patients pregnant more than four months but with local extensive and inoperable cancer.* Here, each patient must be considered from every angle, especially the likelihood of cure by treatment and the desirability of securing a normal child. I cannot lay down any general rule that I myself would follow. Every patient presents a special problem.

Before closing, may I mention that I have seen two cases, in consultation, with bleeding during pregnancy and with what, on gross examination, might have been early carcinoma of the endocervix. Biopsy showed a tissue with the pattern of a grade 1 adenocarcinoma, but without cytologically characteristic changes. These patients were not treated but watched through their pregnancies. The appearance of the cervix, after labor, returned to normal and subsequent developments showed that the condition was not neoplastic.

DR. GEORGE GRAY WARD, New York City.—In the Woman's Hospital, New York, during 15 years (1929 to 1943), there were 27,140 obstetric cases. During this period, we had eight cases complicated with malignancy of the cervix, seven with carcinoma and one with sarcoma. A brief abstract of these cases follows:

CASE 1.—Mrs. C. K., aged 30, pregnant 4½ months, gravida 2, para 2, squamous carcinoma of the cervix and vagina, Schmitz III, 3,600 mg. hours of radium, stillbirth 2 months later, lived 10 months.

CASE 2.—Mrs. C. P., aged 36, pregnant 5 months, gravida 8, para 2, squamous carcinoma of cervix, Schmitz III, 3,600 mg. hr. radium, stillbirth 2 weeks later, lived one year.

CASE 3.—Mrs. A. F., aged 35, pregnant 3 months, gravida 3, para 3, squamous carcinoma of cervix, Schmitz III, 4,200 mg. hr. radium, was irradiated and one month later treated by supravaginal hysterectomy and bilateral salpingo-oophorectomy. The patient was well and lived over 5 years, then died of recurrence of the carcinoma.

CASE 4.—Mrs. P., aged 35, gravida 6, para 5, 12 weeks pregnant, carcinoma of cervix, Schmitz II, was treated by high voltage x-ray followed by 4,200 mg. hr. radium, resulting in death and retention of fetus. Thirteen months later, a Wertheim operation was done, taking 2 hr. and 37 minutes and the patient died of postoperative shock.

CASE 5.—Mrs. D., aged 36, gravida 6, para 4; 6 weeks pregnant, positive A. Z. test, carcinoma of cervix, Schmitz III, was treated by 4,200 mg. hr. radium. She developed a vesicovaginal fistula, and cystoscopy showed invasion of the bladder. She had a missed abortion, lived 9 months and then died of carcinoma.

CASE 6.—Mrs. E., aged 41, gravida 5, para 4, 28 weeks pregnant, squamous carcinoma of cervix, Schmitz III, was treated by a Porro-cesarean section, with a living child. She then was given radium 3,938 mg. hr., and deep x-ray therapy. One year later, she developed stricture of the left ureter and 16 months after the Porro operation a beginning intestinal obstruction. She lived 2 years and died of recurrence of the cancer.

CASE 7.—Mrs. D., aged 26, para 1, was pregnant full term, when a polyp was found protruding from the cervix. An extraperitoneal cesarean section was done with a living child. The pathological report showed the polyp was sarcoma. The treatment was by radium 3,000 mg. hr., deep x-ray and complete hysterectomy. At her last follow-up, 8 months postoperation, the patient was well with no evidence of disease.

CASE 8.—Mrs. C. L., aged 25, gravida 5, para 2, 7½ months pregnant, squamous carcinoma of cervix, Schmitz III, was treated by Porro-cesarean section with delivery of a 4-pound, 15-ounce living girl. At operation, there was infiltration of the right broad ligament and right uterosacral ligament. A high amputation of the cervix was done with no dissection of the bladder peritoneum. Nineteen days later, 2,984 mg. hr. of radium were given and two series of deep x-ray followed, each 3,600 roentgens. The patient and child are now alive and well over 12 years with no evidence of disease.

I believe that for these cases a supravaginal hysterectomy followed by radium and x-ray is the preferred treatment at all stages of the pregnancy. In an early pregnancy, while death of the fetus from the irradiation occurs, it is frequently not expelled, or may cause hemorrhage or infection. The Porro operation, when there is a viable child, is not open to question. In the early pregnancies where there is no possibility of a living child, if a high amputation of the uterus and adnexa is done, we also get the benefit of early castration as an inhibiting factor.

DR. F. H. FALLS, CHICAGO, ILL.—One of the important points brought out by these papers and the discussion is the paucity of cases that we have for evaluation. This possibly depends on the failure to recognize the cancer during pregnancy. When these cases are first diagnosed after the pregnancy, one is inclined to forget that they were recently pregnant and hence, they appear statistically as simple cancer of the cervix.

Some years ago, Dr. Danforth reported 4 cases of cancer of the cervix in pregnancy before the Chicago Gynecological Society. Last year Dr. Fitzgerald, in the same Society reported 6 cases that had occurred at the County Hospital within two years. These cases had been immediately recognized when they began to bleed. Now, unfortunately, when bleeding occurs in a pregnant woman, a "vagina phobia" develops among obstetricians. The patients are put to bed and treated expectantly. The obstetricians do not put specula in the vagina and therefore they do not diagnose cancer. Until we change this attitude of mind and examine every woman who is bleeding during pregnancy, even if it is only a spotting, we will not discover these cases in an early stage.

Another question that came up in Chicago in connection with the cases referred to was whether to do a Porro-cesarean section or an ordinary cesarean section with the object of leaving the uterus so that x-ray and radium could better be given. There was a difference of opinion, but in most of the patients, the uterus was left in. Personally, I thought that this would result disastrously because of infection, but was surprised to find that these patients went along without developing serious infections.

DR. WILLIAM C. DANFORTH, EVANSTON, ILL.—In the report made by me some years ago, four cases of carcinoma of the cervix were discussed. In reference to the cases referred to by Dr. Falls which were discussed at the Chicago Gynecological Society, it was a notable fact that a number of these cases were seen during pregnancy, one case as early as four months, at which time a lesion was definitely seen but not recognized as carcinoma. This emphasizes a most essential point in the management of these cases. Early recognition is vital. Physical abnormalities in pregnancy require the same attention as at other times and biopsy should not be avoided. By early recognition not many opportunities for cure are lost.

As for treatment, it seems to me that when women with carcinoma of the cervix are seen at term the preferable procedure is section followed by amputation of the body of the uterus and later irradiation, both by radium and by x-ray. Women in whom the carcinoma has invaded to any degree should not be permitted to go into labor, first because of the danger of hemorrhage, second, because of the danger of extending the carcinoma by pressure, and third, because of the risk of infection.

DR. MUSSEY (closing).—Search of the literature did not reveal another case of sarcoma of the cervix complicating pregnancy, so that it was especially interesting to have Dr. Ward's comments on his case. None of the cases in our series presented themselves simply because of pregnancy. All were admitted because the cancer had been found by their family physician or else because they had developed symptoms of cancer.

We do not try to draw conclusions as to the best methods of therapy except to say that our best results have been obtained with total hysterectomy by the Wertheim method. The number of cases is too small to reach any final decision.

DEATHS IN GYNECOLOGY*

A Five-Year Analysis of 401 Fatal Cases From Charity Hospital of Louisiana at New Orleans

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(From the Department of Gynecology of the Tulane University School of Medicine)

THE late Dr. John O. Polak,¹ at the 1928 meeting of the American Gynecological Society, read a very frank and honest, and therefore very troubling, paper entitled, "What Can We Learn From a Study of Mortalities?" What he and his co-author learned was that perhaps three-fifths of the deaths which followed their own elective gynecologic surgery, as well as a number of deaths in other categories, might have been prevented by stricter adherence to the criteria which they themselves had set up to safeguard their patients and by a generally better exercise of that intangible faculty which we call surgical judgment.

I think that ever since I read that paper I have been planning to write a similar one when I were old enough in years, and when I thought I had achieved at least a minimum of professional wisdom. For the past year, I have been gathering the material which I am presenting today, and I can truthfully say that it is one of the most profitable exercises I have ever set for myself. My analysis of the 401 consecutive gynecologic deaths (Fig. 1) which occurred at Charity Hospital of Louisiana at New Orleans in the years 1937 to 1942, inclusive, was carried to completion before identification of the services on which they had been handled or of the gynecologists who had handled them. Although they occurred on all the services of the hospital, 40 per cent of all gynecologic admissions are assigned to the Tulane University School of Medicine, and the ultimate responsibility for the gynecologic service of that school is my own.

As a result of this analysis, my former pride in my own service is now tempered with a wholesome humility, and if I ever had any pride in my own personal performances, it is gone. Not a few of the cases on which I wrote "Error of judgment" or "Poor surgery" or occasionally "Gross mismanagement" proved, on identification, to be cases which I myself had either supervised or managed throughout. Whatever be the errors and failures in this series of fatalities, they are not the responsibility of any single service or any single surgeon. All of us need to confess our sins, and our confession should include the commission of things which we ought not to have done, as well as the omission of things which we ought to have done.

The series includes every death at the New Orleans Charity Hospital in the six years ending December 31, 1942, in which a gynecologic state was the primary pathologic lesion. Immediate postabortal states, al-

*Read at the Sixty-Eighth Annual Meeting of the American Gynecological Society, June 19 to 21, 1944, Hershey, Pa.

though they are often included in such studies, were excluded. I should like to make it clear that behind the statements made and the conclusions drawn, which may sometimes seem sweeping, is a great mass of statistical data. Their analysis was necessary for my purposes, but the details are not presented because I am not interested in statistics as such.

The preponderance of Negro cases in this series (Fig. 2) can be explained in a variety of ways: 1. Certain diseases, such as pelvic inflammations and uterine fibroids, are actually more frequent and are usually more severe in Negroes, who are even more inclined than white persons to neglect all illness in its early stages. 2. Negroes have not shared equally in the general prosperity which recently has reduced the number of white admissions to charitable institutions all over the

AT CHARITY HOSPITAL OF LOUISIANA AT NEW ORLEANS 1937-1942

OF EVERY 20 PATIENTS WHO DIED OF GYNECOLOGIC CAUSES



(12) DIED OF MALIGNANT DISEASE, OF WHOM



8 DIED OF CARCINOMA OF THE CERVIX ;



—AND—

(8) DIED OF BENIGN DISEASE, OF WHOM



3 DIED OF PELVIC INFLAMMATORY DISEASE, AND



3 OF UTERINE FIBROIDS.



Fig. 1.

country. Even if they had, in this community at least, they could not be cared for in the existent facilities for their race. 3. For the same reason, though this fact also explains a certain number of white hospital deaths, Negroes show disproportionate admissions to Charity Hospital for terminal care in malignant disease; they have literally nowhere else to go in their final days of life.

The age differential apparent in this series is usually noted in comparative studies of benign and malignant disease, though a breakdown of the figures would show that Negro deaths, particularly from malignant disease, tend to occur somewhat earlier than do white deaths.

An Analysis of 247 Deaths From Malignant Disease

Deaths from malignant disease make up almost two-thirds of these 401 fatalities (Fig. 3), and deaths from carcinoma of the cervix, which

numbered 167, make up well over two-thirds of the deaths from malignant disease. Eight of the 29 deaths from malignancy of the uterus were due to sarcoma, which in 6 cases originated in uterine fibroids. Fibroids were also associated with 6 cases of fundal malignancy. Incidentally, 7 of the 247 patients who died of malignant disease presented double malignancies, and an eighth patient, who seemed biologically

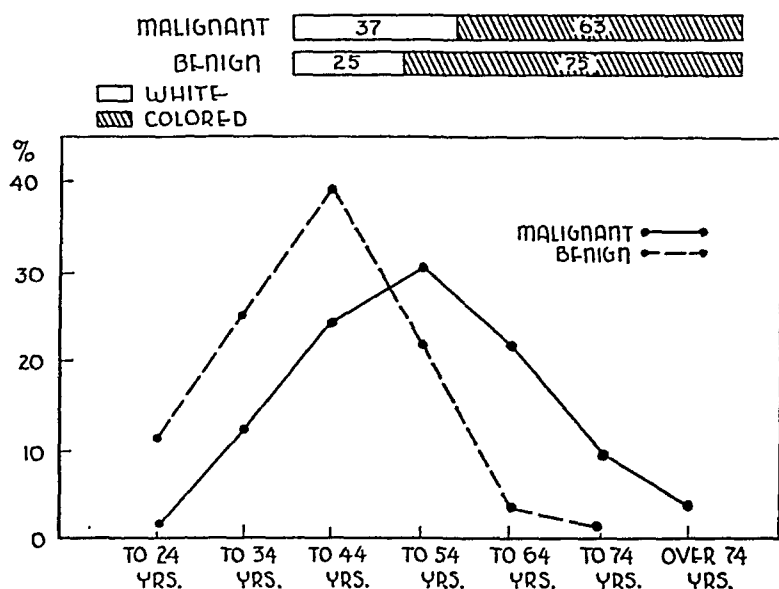


Fig. 2.—Distribution according to race and age of 401 gynecologic deaths at the New Orleans Charity Hospital 1937-1942.

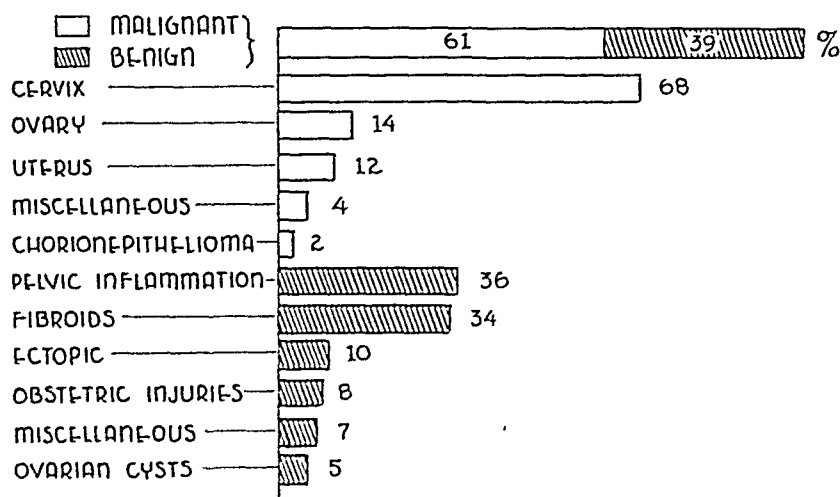


Fig. 3.—Proportionate distribution of pathologic lesions in 401 gynecologic deaths at the New Orleans Charity Hospital 1937-1942.

doomed to die of cancer, finally died of carcinoma of the vulva, after surviving operations for carcinoma of the rectum and for carcinoma of different histologic characteristics in the right and the left breast.

An analysis of these cases, and particularly of the cases of carcinoma of the cervix, emphasizes the fallacy of relying upon generalities and laws of averages and similar considerations for diagnosis. Carcinoma

and sarcoma are predominantly diseases of middle life, it is true, but 25 of the 167 deaths from carcinoma of the cervix, for instance, occurred in women under 39 years of age, and 5 of these in women under 29 years of age. Carcinoma of the cervix is overwhelmingly a disease of parous women, but in the 157 cases in which these data were available, 2 women were unmarried, 11 were sterile, and 3 had had only abortions. In 3 other instances, the confusion in which I leave to your imaginations, the onset of symptoms of cervical malignancy coincided with or followed immediately upon pregnancy or abortion.

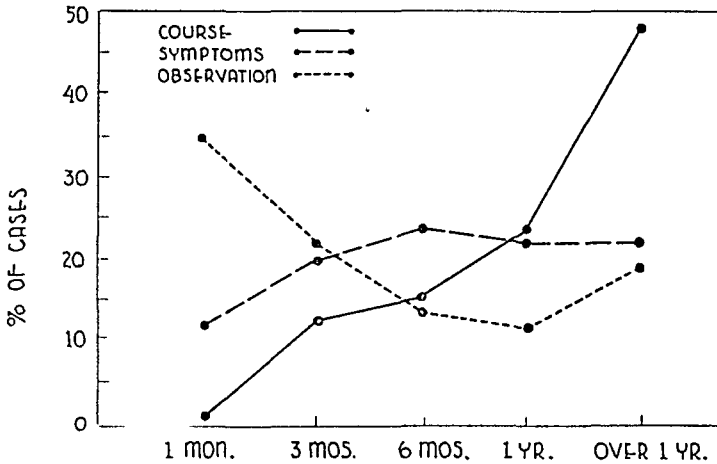


Fig. 4.—Proportionate distribution according to total course, duration of symptoms before medical consultation, and duration of observation in 247 fatal cases of various types of pelvic malignancy at the New Orleans Charity Hospital 1937-1942.

As to symptoms, it is true that a discharge, or irregular bleeding, or a combination of these symptoms is usually the first indication of the presence of most types of genital malignancy, but reliance upon them is fallacious. In these cases, diagnosis was sometimes confused and delayed because the first symptoms were pain in various locations, rectal and urinary difficulties, dyspareunia, general symptoms such as loss of weight and malaise, and bizarre symptoms such as distention, chills and fever, and fecal and urinary incontinence. The picture of ovarian malignancy was various and completely atypical. Only abdominal enlargement, which practically always indicated a fluid collection, was common to all cases, and in many instances the first symptoms were referred to the urinary or intestinal tract, or to the chest. One of the most curious features of this study was the eight cases in which a blow, a fall, or another illness (including, in one instance, extraction of teeth) from which she did not fully recover, first called the patient's attention to her genital disease. The facile statement that many of the symptoms I have listed are late symptoms is not helpful; if they are the first symptoms of which the patient is aware, that is all the worse for the patient and her chances of recovery, but they must be evaluated as such.

Many of these cases suggest that the supposedly physiologic years of the climacteric are in many respects the most dangerous period of a woman's life. Not only the patients themselves, but in most instances

the private physicians whom a few of them consulted, and in an occasional instance the hospital staff, regarded spotting and bleeding and frank hemorrhage as part of the menopause, and in some cases no pelvic examination was made for the paradoxical and incredible reason that the patient was bleeding.

Graphic presentation in these 247 fatal cases (Fig. 4) of the relative duration of illness, of symptoms before hospitalization, and of observation shows that in a fair number the hospital cannot reasonably be charged with the responsibility for the fatalities. In carcinoma of the cervix, for instance, though the known duration of observation ranged from eight hours to something over seven years, more than two-thirds of the patients were observed less than a year, of whom 26 were under

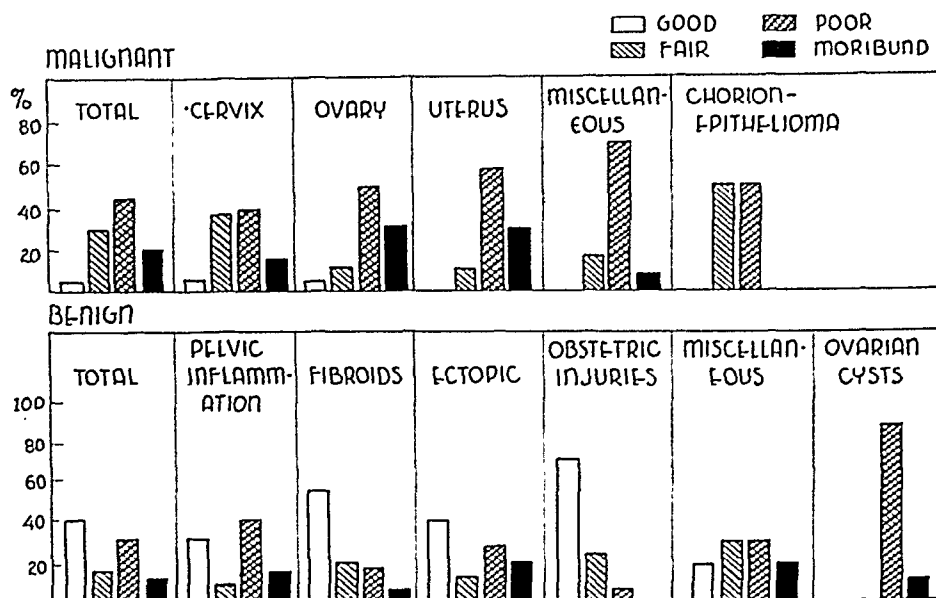


Fig. 5.—Proportionate distribution according to status of patients of 401 deaths from gynecologic causes at the New Orleans Charity Hospital 1937-1942

observation less than three months, 32 others less than a month, and 12 others less than a week. The known duration of symptoms prior to observation is equally revealing: Considerably less than half of the patients for whom these data are available sought medical advice within a year of the development of symptoms. Furthermore, what has been said of carcinoma of the cervix can be applied without much qualification to all other varieties of malignant disease.

The results of these circumstances are reflected in other cases. From the standpoint of their physical status (Fig. 5), only a small number of these patients were in good condition, and less than a third were in a fair state of health. To state the facts in reverse, 44 per cent of these patients were in poor condition and something over 20 per cent were actually moribund. In carcinoma and sarcoma of the fundus, to use a specific illustration, 17 of the 29 patients were in poor condition when they were first seen, and nine were moribund. In the 141 cases

of carcinoma of the cervix in which it was possible to determine from the records the clinical stage of the disease, 15 patients were classified as Stage I and 14 as Stage II. Being interpreted, those figures mean that approximately four-fifths of the patients who died of this disease were not in the two clinical groups in which there is any reasonable expectation of long-term salvage. There is no point to a discussion of the histologic types of cancer and their response to therapy when one is dealing with such a background as this.

The therapy of this group of cases is about what would be expected under these circumstances (Fig. 6). In the entire group of 247 patients, only 15, 6 per cent, all of them women with carcinoma of the cervix, received optimum therapy for their disease. In well over a third of all cases of malignant disease the only possible treatment was symptomatic, chiefly directed to the relief of pain and the control of hemorrhage.

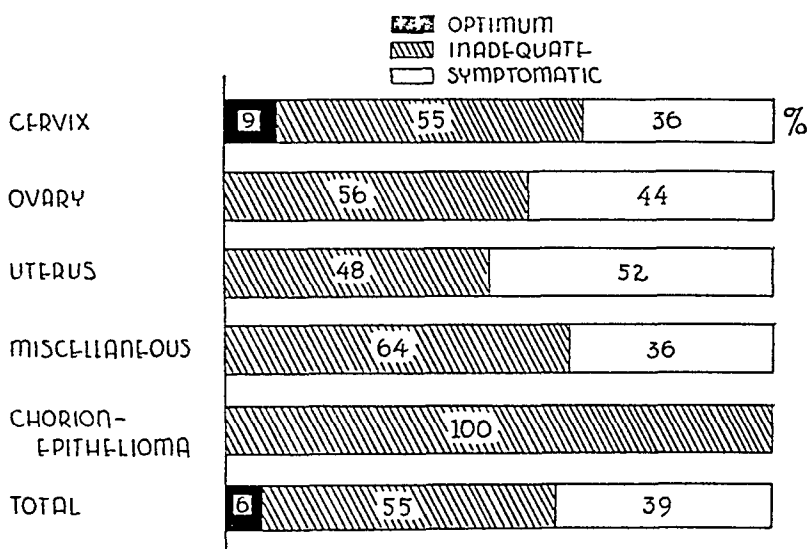


Fig. 6.—Proportionate distribution of therapeutic measures in 247 deaths from pelvic malignancy at the New Orleans Charity Hospital 1937-1942.

Under the circumstances, it would be almost a mockery to discuss ideal plans of therapy for the various types of malignant disease.

In this connection, let me say that I applaud the motive which underlies the performance of palliative surgical procedures in malignant disease, and in the occasional case I have no doubt that they are justified. But on the whole I question, when a patient has advanced to the stage at which the intestinal or urinary stream is interfered with, whether enough can usually be accomplished by such procedures to justify their performance. My own idea is that it is better to make the patient's last days comfortable with liberal sedation, supplemented by intravenous fluids if dehydration is annoying, than to add a few months to a life that is not worth living by colostomy, nephrostomy, and similar operations, the most merciful feature of which is that they sometimes precipitate the death which they were planned to delay. For the same reason, though again I appreciate the motive, I see no point whatsoever to the

use of expensive vitamin therapy, transfusion with blood which might better be saved for the living, and similar measures in patients who are dead even before they have died.

The majority of cases in which no curative therapy or in which inadequate curative therapy was applied are made up of cases in which there was delay in seeking medical advice, and in which the patients were in poor condition when they were first seen. There are, however, certain exceptions. In some cases of carcinoma of the cervix, the presence of old pelvic infections contraindicated the application of radium, and in others, the lighting up of such infections made necessary the removal of radium long before a therapeutic dose had been received.

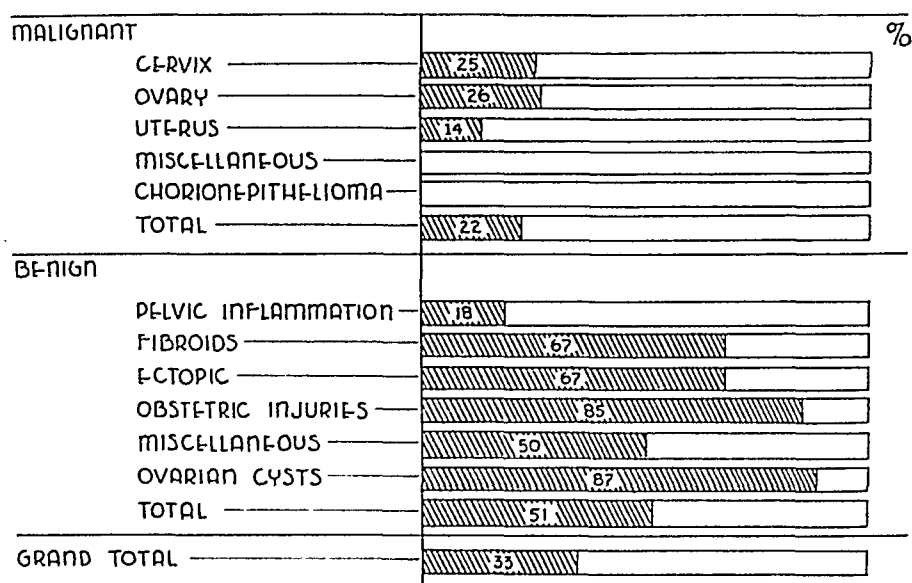


Fig. 7.—Proportionate distribution of possibly preventable deaths in 401 gynecologic fatalities at the New Orleans Charity Hospital 1937-1942.

In several instances, in all classifications of malignancy, the patients' obesity was so extreme that it was doubtful whether deep x-ray therapy were of any value at all. In a number of instances, therapeutic irradiation was well begun, but the patients improved so much that they disregarded instructions as to when to return for observation and further treatment. In a few instances they delayed for more than a year and in one or two instances they delayed for two years or more. With these lapses they signed their own death warrants.

One hesitates to make categoric statements about preventable deaths in malignant disease, but with that qualification it may be said that in a fair number of these cases (Fig. 7) a different course of action, *either inside or outside of the hospital*, might have changed the course of events.

1. For instance, 12 patients with carcinoma of the cervix had consulted physicians outside of the hospital, as had an occasional patient in the other groups and the treatment they received is a sorry

commentary on our teaching and practice. One patient, advised to have a biopsy of the cervix, left the physician who had given that excellent advice and went to a second physician, by whom she was treated medically for two years. A second patient was treated by amputation of the cervix. The other 10 patients either were treated with douches and pills and icecaps and bed rest, frequently without a pelvic examination, or were treated for such diseases—which some of them had in addition to their genital malignancy—as diabetes, hypertension, bacillary dysentery, undulant fever, and pyelitis.

2. Another group of patients, some 25 in all, were under treatment in the clinics or wards of the hospital for periods varying from a few months to several years, for medical conditions, which they actually had, chiefly syphilis and cardiovascular disease. During this time they developed their malignant disease literally under the eyes of the physicians who were treating them for their other diseases. They were either not questioned as to their menstrual habit and genital health, or their statements concerning these matters were not properly evaluated because of absorption in other conditions, and again, and all too frequently, pelvic examination was not a part of the routine of physical examination.

3. In an occasional case in which surgery is the preferred or only treatment for the special type of malignancy in question, operation was not performed, and in one or two cases in which the malignant process was possibly curable, technical errors at operation were responsible for the fatal outcome. In most cases, however, exploration proved that nothing at all could be done, and in a few instances it actually precipitated death, an outcome which no surgeon, if he can absolve himself of carelessness, can find it in his heart to regret. Incidentally, evisceration occurred in 3 of 19 cases of ovarian malignancy in which exploration was done. A number of patients with carcinoma or sarcoma of the fundus associated with uterine fibroids had been told that operation was not necessary, or had refused operation for the benign tumors; they were lost sight of, and returned with inoperable malignancy.

4. Twelve of the 167 patients with carcinoma of the cervix had been submitted to supravaginal hysterectomy from 9 months—when the malignant disease was undoubtedly already present—to 23 years before they appeared with carcinoma of the cervix. Whether or not carcinoma of the stump is favorable or unfavorable for treatment, I am not prepared to say. I am struck with the fact however, that 9 of these 12 patients were in clinical Stages III or IV; that 7 of the 12 were in poor condition or moribund when they were first seen; and that 5 of the 12 were dead within 6 months of the time they were first seen, one of them within 16 days.

I think it fair to say that in every one of these 12 cases the performance of the complete rather than of the supravaginal operation would have eliminated the site in which the malignancy developed. The argument that carcinoma of the vagina may develop after the complete operation I regard as having absolutely nothing to do with the point at issue. Nor can I subscribe to the opinion that because the complete operation in unskilled hands carries a higher mortality than the incomplete we should not advocate it. The policy of such an organization as this should surely be to proclaim standards rather than to practice expediency. On my own service at Charity Hospital we now perform the complete operation routinely in every case in which no contraindication exists, our case fatality rate is actually lower than

for the supravaginal operation, and we thus insure our patients against just such statistics as those I have cited.

5. I hesitate to say that any patient with adenocarcinoma of the ovary can be saved, for I myself have never saved such a patient. I therefore make the statement with many reservations, in view of the terrible swiftness of this disease, that in one or two instances more energetic efforts at diagnosis might have led to earlier operation. In one case in this series, by what proved a tragic error of judgment, the ovaries were resected, in an attempt to be conservative in a young woman, and the error was compounded by failure to make use of the pathologic report of malignancy until it was too late to remedy the mistake. In another case of papilocystadenoma peritoneoscopy, which I personally regard as far more radical than exploratory laparotomy, resulted in puncture of the jejunum; prompt recognition of the accident and repair of the bowel failed to save the patient's life.

6. A bolder attack on one or two cases of carcinoma of the vulva might possibly have given the patients a chance of life which they did not have with nonsurgical measures, but I doubt it. Two of the 6 cases of chorionepithelioma were frankly mismanaged, but in each instance the disease was so far advanced that the mistakes made no difference.

7. I think it worth emphasizing, though the error was not made in any case in this series, that too much reliance upon the pathologist, whose word should usually be the court of last resort, can be misleading. In one case of chorionepithelioma, for instance, the Friedman test, though performed by all techniques including the fractional, was always negative. In some cases of carcinoma of the cervix biopsy, quite properly, was omitted. The necessary manipulations might have caused serious bleeding, and there was, above all, no justification for disturbing dying women to secure a merely academic confirmation of a diagnosis that was obvious. On the other hand, in 8 of the 126 cases in which biopsy was taken, the specimen was reported negative once, twice or several times, one specimen never being reported positive. When there are sufficient clinical grounds for the belief that the process is malignant, the institution of therapy in the absence of a laboratory diagnosis is certainly justified, and under no circumstances should such a patient be dismissed from observation, for any delay in treatment may be sufficient to seal her doom.

An Analysis of 154 Deaths From Benign Gynecologic Disease

I had believed, before I analyzed them, that the 154 deaths in this series due to benign gynecologic disease would prove very nearly 100 per cent of them to be inevitable. I was basing my opinion on the improvement in results which I have observed in my own time. In a recent study I have shown how the case fatality in pelvic inflammations has been cut in half in recent years. I knew that on my own service in 1943, there were only two deaths in 357 hysterectomies. An analysis of the individual deaths in this series, however, left me with considerably less reason for pride.

The majority of the 154 deaths (Fig. 3) were due either to pelvic inflammation (55 cases), or to uterine fibroids (53 cases). For the reasons already stated (Fig. 2), the majority of deaths in each category,

42 and 43 cases, respectively, occurred in Negro women. It is also worth noting that in the fibroid group 12 of 14 women under 34 years of age were Negroes, as were 9 of 12 women under 39 years of age.

Both of these diseases are ordinarily regarded as conditions which do not kill per se. It is not altogether surprising to New Orleans gynecologists, however, to find (Fig. 5) that a large number of the women with pelvic inflammation and a smaller number of the women with uterine fibroids were in poor condition, while 9 in the former and 4 in the latter group were actually moribund. Surgery may or may not be indicated in pelvic inflammations, but the condition of 12 patients with that disease was such that only symptomatic treatment was possible. Uterine fibroids is a disease in which surgery is usually the desired treatment, but 7 of these 53 women were in such condition that operation could not be considered, and in one instance the only possible procedure was simple excision of a prolapsed, sloughing submucous fibroid. Many of the Negro patients had had their growths for years, so that they had reached enormous size and had become complicated by adhesions and various forms of degeneration. Hypertension and cardiac or cardiorenal disease added to the risk in some of these cases, and obesity was a complicating factor in 9 patients, one of whom weighed more than 300 pounds.

1. On the other hand, operations for fibroids are almost never anything but elective, in the sense that there is almost always time for adequate preparation, so that a woman who is originally a poor risk can be converted into a fair one, or a woman who is only a fair risk can be made into a better one. Analysis of the individual cases in this series shows (Fig. 7) that in perhaps 37 of the 53 deaths due to fibroids, and in perhaps 10 of the 55 deaths due to pelvic inflammatory disease, the fatality might have been avoided. A study of these presumably preventable deaths revealed such avoidable errors as inadequate investigation; poor preoperative preparation or none at all; poor or delayed or inadequate or too brief postoperative therapy; lack of alertness in detecting postoperative complications in their incipiency; uncorrected anemia; prolongation of the operative time beyond the limits of safety; excessive blood loss at operation; and, particularly in fibroids, a rather general tendency to underestimate the possible risk.

In the fibroid cases, to illustrate, technical errors were responsible in 4 cases for injury to the bladder, rectum or ureter. In 1 case, on my own service I regret to say, far too much surgery was undertaken at one time in a patient in poor condition. Prophylactic appendectomy was ill advised in three cases, in one of which it was done in the face of the internist's warning that the patient was a poor risk and surgery should be kept to the minimum. In at least 10 of the 16 deaths from peritonitis, and in perhaps 2 of the 6 deaths from embolism, there is a strong possibility that better treatment before and after operation might have averted the fatality. Incidentally, evisceration occurred in 4 of the 46 surgical cases in this group.

Special mention should be made of 7 surgical cases in the fibroid group, all proved by post mortem, in which the only clear cause of death was liver failure or the liver-kidney syndrome. In 6 of these,

as a review of the histories shows, hepatomegaly or other considerations indicated, at least in retrospect, the necessity for tests of liver function, which were not carried out in any instance, and for preoperative preparation directed toward the liver. It is curious that although in several instances this syndrome after operation was, on review of the cases, perfectly typical, it was not suspected in a single instance, although in most cases a systematic exclusion of other possibilities left the patients' condition a diagnostic puzzle.

2. In the group of deaths due to pelvic inflammation, the abdomen was opened in 3 cases in which colpotomy might have been wiser. Conization of the cervix, which was carried out in 1 case, is a procedure of dubious wisdom in the presence of intra-abdominal infection. Extraction of the teeth, however necessary in itself, seems to have little justification as a preoperative measure in a woman seriously ill with pelvic infection.

To me, the most astonishing finding in the cases of pelvic inflammation was that of 38 instances in this category of tubo-ovarian or other pelvic abscesses; rupture had occurred in 14, as demonstrated by autopsy, and seems to have occurred, on the basis of sound clinical evidence, in 7 others. These 21 cases are exclusive of the cases in which rupture occurred at operation, as the result of manipulation, but include 1 instance in which the rupture followed so closely upon bimanual examination that a cause and effect relationship seemed perfectly reasonable. Some of the patients were moribund on admission and apparently had suffered their ruptures some time before. In some instances, rupture occurred in the hospital, literally under the eyes of the staff. One patient, in apparently good condition, was refused admission to the hospital and directed to return for operation after bed rest at home; she suffered her rupture on the way home, and returned to the institution in deep shock two hours later. These deaths, together with certain other deaths in which surgery seems to have been postponed much too long, can fairly be classified as preventable.

3. Ectopic pregnancy was the cause of death of 15 patients, 9 of whom were not submitted to surgery. This is a truly startling situation, for of all emergency gynecologic conditions, none responds more promptly and more satisfactorily to surgical therapy than does this condition. Though some patients were in advanced stages when they were first seen, diagnostic confusion by no means explains every case. In 5 cases in which the diagnosis was made absolutely or tentatively, therapy, which should always be promptly surgical, was hesitant and long delayed. In 3 cases no donors were ever secured, and in 6 others the efforts to secure them were late and curiously languid. In a single case of full-term abdominal pregnancy, the placenta, although very adherent, was removed, with immediate furious and fatal hemorrhage.

These deaths are more to be regretted because 6 of the 15 patients were in good and 2 were in fair condition when they were first seen. It is true that 3 were moribund and 4 were in poor condition, and it is also true that rehabilitation of a patient to the point where she is out of shock is ordinarily a laudable plan of procedure. But ectopic pregnancy is one condition in which I think the contrary is true. I intend no invidious comparisons, since some of these deaths were the responsibility of my own service, when I say that I think that in most of the 15 cases I should myself have operated instantly to tie the bleeding point, letting the patient take her chances of rehabilitation later, when I think they would have been greatly improved. I make the statement the more

emphatically, for in 2 patients who were moribund, I, myself, operated under such circumstances, and in each instance witnessed prompt and dramatic recovery.

4. Thirteen patients died whose basic pathology was obstetric injuries, which in 8 cases took the form of prolapsus uteri. This small group of cases is worth analyzing in some detail, for in 12 cases the operations were entirely elective, and the status of the patients was good or fair in all but one instance. In other words, the circumstances in this group were chiefly favorable.

In some 11 of these 13 cases the records suggest that the fatal outcome might have been avoided. For instance, a 31-year-old patient was submitted to vaginal hysterectomy when at her age a less radical procedure would probably have corrected her displacement. A stocky, obese woman, with first-degree prolapse and very short ligaments, was submitted to vaginal hysterectomy when the abdominal route would have been simpler and safer. In 4 instances technical errors were made at operation, in one of which, through a tragic mischance, a ureter was tied. When the abdomen was finally reopened, it was found that the other ureter was blocked by the extension of a then unsuspected carcinoma of the pancreas; incidentally, that finding clarified a number of symptoms which had simply been disregarded in the work-up of the case.

In this same group investigation after operation, when an obscure complication developed, revealed a past history suggestive of a central nervous system lesion; I doubt that this patient should ever have been operated on. Several patients might have been benefited by preoperative preparation, of which they had none, and several others by more preparation than they had, including the correction of a hemoglobin deficiency of 50 per cent. In 6 cases, one of which was another instance of apparent liver death, postoperative care was not entirely adequate.

It is evident, I think, from what has been said that more alertness and less complacency on our part might have saved most of these patients. I make the statement with deep regret, for 5 of the 8 cases of uterine prolapse occurred on the Tulane service on which—hitherto, at least—we have rather prided ourselves on our results with vaginal hysterectomy.

5. Of the 8 patients with various types of benign ovarian tumors, prompter investigation and more alert and more adequate preoperative care might have saved perhaps 7. One patient with pseudomucinous cystadenoma was refused immediate admission because of an influenza epidemic; she returned five years later, and in the 26 months before her death, 96½ gallons of fluid were removed from her by repeated paracentesis.

6. I am inclined to believe that perhaps 5 of the 10 remaining cases, in which the diagnoses included tuberculous peritonitis, pyometrium, uterine polyp, and endometritis, might have been saved by a wiser choice of procedure and more attention to preoperative and postoperative care. It is only fair to point out, however, that 3 of the patients in this group were in poor condition when they were first seen, and that 2 others were moribund and died within 48 hours.

Comment and Conclusions

The general impression received from a study of these 401 deaths is that, on the whole, the cases were well managed from the standpoint of the hospital, and that in the great majority of cases, particularly

the malignancies, and after making due allowance for the speed and general hopelessness of such conditions as adenocarcinoma of the ovary, the patients were responsible for their own deaths. On the other hand, in perhaps 25 per cent of the deaths from malignant disease the patients might have been given a chance of life, and in perhaps half of the deaths from benign disease the outcome might have been different, if the plan of management *outside as well as inside of the hospital* had been different in some or in all respects.

1. Histories should be taken with much more care from every standpoint. In several instances in this series detailed knowledge of past episodes of cardiac, renal and other diseases would have meant re-evaluation of the operative risk, and in a few instances treatment by non-surgical measures.

2. There should be less complacency about the risk in both uterine fibroids and pelvic inflammations. In both diseases the case fatality rate is now gratifyingly low, but only such an analysis as this reveals that a low case fatality rate does not mean that all of the patients who died could not have been saved. Neither disease is always as simple as it seems. In this series, the responsibility for the cases in which there was an unwise estimation of the risk was about equally divided between the surgeon and the medical consultant. The medical consultant sometimes seemed rather too optimistic about the patient's status, and the surgeon, for the same reason, sometimes disregarded the consultant's warning as to the duration of operation and the type of anesthesia.

3. In all surgical cases there could well be a more careful evaluation of the need for preoperative therapy, even when the patients seem fair risks and present only minimal deviations from the normal. Blood surveys should be carried out in all cases, and mild degrees of anemia, hypoproteinemia, urinary tract disease, and hepatic dysfunction should be investigated and corrected as necessary, since minimal deviations from the normal tend to become maximal if unexpected technical difficulties develop, or if unusual blood loss occurs at operation. General measures, including a period of bed rest in hospital before operation, will usually convert a fair risk patient, who presents no tangible deficiencies, into a better risk.

4. There should be more alertness after operation to detect possible complications in their incipency, more speed in instituting treatment when such complications are discovered, and a quicker resort to such measures as intestinal decompression, infusion, transfusion, and oxygen therapy when it is evident that less active measures are not achieving results. Such measures, furthermore, should be continued until it is clear that improvement has occurred and should not be discontinued when it is merely hoped that it is occurring. Particularly to be guarded against is too early a return to oral feeding in ileus and peritonitis.

cluded. The fact that in most instances in this series their diagnostic lack of suspicion made no difference does not in the least alter our responsibility as to how these men are taught.

10. Interns and residents in particular must be imbued with the belief that not all instances of malignant disease are hopeless, an idea which a surprising number of them now seem to possess, and which results in an eager desire to clear the wards of such cases and to use the beds for other purposes. They must be further impressed with the idea that much can be done for the comfort of such patients, even when cure is not to be expected. On the other hand, when it is evident that they will merely prolong a life that is not worth living, transfusions, vitamin therapy and similar measures should be promptly discontinued. For the same reasons, most palliative surgical procedures have a very limited field of usefulness.

11. For frank errors of diagnosis and treatment we are, of course, responsible as individuals, and most of the preventable deaths from benign disease in this series fall into that classification. But hospital errors do not account for more than a small percentage of the possibly preventable deaths from various types of pelvic malignancy in this series. How much responsibility shall we assume for the great body of patients with pelvic malignancy who fail to seek medical aid until it is too late to help them? Personally, I think we shall have to assume a large share, and we shall have to meet it by an improvement in our teaching methods, such as has already been outlined, and by an even greater improvement in our propaganda methods, which at present are clearly ineffective.

As many of these cases show, the menopausal years are a period of particular danger in a woman's life because of the possible confusion between the expected irregularities of those years and the early symptoms of malignancy of the cervix. The solution would seem to lie in teaching women to submit to pelvic examination at regular intervals, whether or not they present symptoms. If proof of that policy were needed, Macfarlane and her associates in Philadelphia² have recently provided it. The criticism that they found only 4 malignancies of the cervix in their first 955 pelvic examinations, all of which were carried out on women in whom there was no reason to suspect malignancy, or that they found no instances of malignancy in their next thousand-odd examinations, is no criticism at all. The point is that by routine examination of all women willing to be examined, Dr. Macfarlane and her associates found 4 early malignancies of the cervix which otherwise would probably not have been found until later. It is not too much to say that those 4 women owe their lives to this courageous group of physicians. The plan that they are putting into practice seems the simplest, and indeed the only practical, way to improve the present disastrous results in genital malignancy, and more of us would do well to employ it.

Another form of propaganda is also necessary. Physicians as well as patients must be taught the potentialities for danger in vaginal discharges and menstrual irregularities. Physicians, including gynecologists, should be taught to welcome the opportunities to make routine examinations, in the absence of symptoms, rather than to discourage them, as has been done in more than one instance of which I have knowledge. At the present time, gynecologists seldom see these women until their symptoms are clear-cut and their disease is correspondingly advanced. Their family physicians see them first.

I know of no more effective, and at the same time no sadder, way to conclude this paper, in which my only aim has been to point the road to improvement, than with the statement that with one single exception, every patient in this series with malignant disease who had consulted a physician before she came to the hospital received advice that was lethal. It is one of life's ironies that the single patient who was advised to submit to biopsy declined the investigation and went to a second physician, by whom her carcinoma of the cervix was treated by medical measures for almost two years.

Summary

An analysis of 401 consecutive deaths from gynecologic causes, two-thirds of which were due to malignant disease, has been presented from the standpoint of how many were positively or possibly preventable. The various considerations by which some of these fatalities might have been prevented are discussed.

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Discussion

DR. NORMAN F. MILLER, Ann Arbor, Mich.—It is illuminating and helpful to hear something about the bad as well as the good results in the management of our cases. Today, we have been fortunate enough to have two papers which fall into this category. This morning Dr. Huber told us about the deaths in his eclampsia cases, and this evening Dr. Miller tells us about deaths occurring on his gynecologic service. It takes courage to tell about bad results and both of the speakers should be congratulated on their frankness.

One of the outstanding things about Dr. Miller's paper is the fact that it shows us again that our number one problem in gynecology is cancer. Sixty per cent of the deaths among his patients were in this category. The fact that so many cases were far advanced is a characteristic finding for all cancer clinics, and it emphasizes once more that whether we like it or not, we still have a very important educational problem before us. Sometimes educational endeavors for the laity seem decidedly fruitless, but though progress is slow, we must not let down in our efforts.

Dr. Miller makes a rather surprising statement to the effect that to his knowledge, he has never cured a case of ovarian adenocarcinoma. Certainly such a statement emphasizes the seriousness of that disease and also points to the value and help that might accrue to women through periodic health examinations.

Another point of interest is the report of 12 deaths due to cervical stump carcinoma. I think we all agree that in patients requiring hysterectomy, total hysterectomy is the operation of choice provided there be no contraindication to complete extirpation.

I was also surprised to learn that there were 15 deaths from ectopic pregnancy, 9 of three patients had not been operated upon. Recently, I discovered that some of the best men in my own state favored expectant treatment of ectopic pregnancy. In our experience, delay is seldom justified.

I am sure we can support Dr. Miller in his conclusion wherein he states that greater attention to preoperative examination and preoperative preparation of the patient is to be repeatedly emphasized. No patient will object to such care when she realizes that these additional measures are being undertaken for her safety.

DR. CATHARINE MACFARLANE, Philadelphia, Pa. (by invitation).—Dr. Miller mentioned the research on the control of cancer of the uterus which is being conducted at the Woman's Medical College of Pennsylvania. In this connection I should like to report that of the original group of 1,319 volunteers, 550 have completed the five-year period of examinations.

Three early cancers of the uterus were discovered in the first round of examinations. These volunteers were treated with radium and are well five and six years after treatment. A fourth early cancer was discovered on the tenth visit of another volunteer. This lady was treated with radium and is well 15 months after treatment.

The discovery of these four early cancers in presumably well women furnishes an argument in favor of periodic pelvic examinations.

DR. THADDEUS L. MONTGOMERY, Philadelphia, Pa.—The discouraging results which Dr. Miller refers to in the field of gynecologic cancer lead quite logically to the questions, first, of the role of periodic gynecologic examinations in the prevention of disease or its early recognition, and second, to the matter of better education of our medical students and young doctors in gynecologic diagnosis.

While I cannot judge, of course, how widespread the influence of Dr. Catharine Macfarlane's campaign for regular examination has been throughout the country, I can say that in Philadelphia, women are conscious of the importance of periodic health examination. If the doctor does not of himself recommend it, they ask for it. For this enlightened state of mind in our home city, I believe that Dr. Mcfarlane is largely responsible.

As a result of this newer development in gynecology, 20 to 30 per cent of our office work is now made up of semiannual and annual gynecologic examinations. I can foresee the time not far distant when this phase of activity, properly encouraged, will constitute the majority of our office work. The time has arrived when no obstetric patient, no new gynecologic subject, and no postoperative patient should be discharged without the recommendation of a semiannual checkup. If every practicing obstetrician and gynecologist would, upon these occasions, avail himself of the opportunity of spreading this bit of lifesaving propaganda, the word would soon get about to all the women of the country.

The second proposition is the better training of our medical students and young physicians in the early recognition of the common and serious gynecologic diseases. For this there is now some hope. The young doctor is "cancer conscious" and the divisions of gynecology in the various medical schools of the country are doing a much better job of instruction than formerly. Most of such departments have given up their former undertaking to make gynecologic suregons out of the fourth-year medical students and are devoting their teaching hours much more profitably to methods of diagnosis and office treatment. The significance of irregular vaginal bleeding is emphasized over and over again.

AN ANALYSIS OF 101 FATALITIES FROM ECTOPIC PREGNANCY*

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(From the Committee on Maternal Welfare, Philadelphia County Medical Society)

IN THE decade, 1931 to 1940, which was characterized by a nationwide activity in maternal welfare, the incidence of deaths from ectopic gestation to total puerperal deaths in Philadelphia was 5.7 per cent, in New York 6.3 per cent, and in Chicago, 8.1 per cent. Expressing the figures in another manner, every eighteenth puerperal death in Philadelphia, every sixteenth puerperal death in New York and every twelfth puerperal death in Chicago during this period was due to ectopic gestation.

In Philadelphia among 2,204 ectopic gestations recorded by the hospital record librarians and the Coroner's office, from 1931 to 1943 inclusive, there were 101 deaths, a mortality of 4.6 per cent.

Coincident with the reduction in the maternal mortality rate locally during these years, there has been a definite improvement in the management of ectopic gestation. Sixty-two of the deaths reported occurred during the first six years of this study and 39 during the next seven years. The mortality per number of ectopics reported in the first six years was 5.6 per cent, and for the next seven-year period only 3.5 per cent. In the last two years the rate was 2.2 per cent.

Since 1931, the Committee on Maternal Welfare of the County Medical Society has analyzed individually every maternal death in Philadelphia. When the number of ectopic gestation deaths, 1931 to 1943, reached 101, it was felt an analysis of the histories might prove of value. The following factors were considered in this analysis:

Age.—Thirty-eight deaths, the largest number in a single age group, occurred from 30 to 34 years. The percentage of these deaths to the entire series, approximately 38, is double the distribution of total births, 19 per cent in the same age group over a twelve-year period in the city. Twenty-four per cent of the deaths occurred in the age group, 25 to 29 years, the group in which 30 per cent of the total births occurred. It is probable that the increased incidence in the ages 30 to 34 years may reflect repeated pelvic assaults of pregnancy, abortion or infection.

Race.—Thirty-eight per cent of the ectopic gestation deaths occurred among Negro women. Approximately fifteen per cent of the total births in the twelve-year period occurred among Negro women. Ectopic gestation to total puerperal deaths in the Negroes was 9 per

*Read at the Sixty-Eighth Annual Meeting of the American Gynecological Society, June 19 to 21, 1944, Hershey, Pa.

cent, just twice the ratio in white puerperal deaths. These contrasting percentages may be due to a greater incidence of pelvic infection in the Negro race.

Parity.—In the women whose parity was known, 30 per cent of the series had not been pregnant before. Of the remainder, 16 per cent had had one previous pregnancy, and 23 per cent two previous pregnancies.

Present History.—A history in this study of ectopic gestation has been regarded as typical if there was amenorrhea associated with vaginal bleeding and abdominal pain. There were 30 cases where such a history was obtained.

In 49 instances such a typical triad of symptoms was less well defined. We have regarded as a suggestive history one which may or may not have included absences of menstruation, but where low abdominal pain and vaginal bleeding were present and should have helped toward a true diagnosis.

Misleading, chiefly falsified, histories were present in 12 cases, particularly where attempts at criminal abortion had been made, or where the patient was unmarried.

In ten cases, no history at all was obtained. It should be remarked that in our maternal mortality study in Philadelphia not only are the hospital records available, but interviews by the recorder of the Committee are had with local physicians and the family. In many instances, the statements of the family to the Coroner's office have given us the history of the case.

We have stated in discussing parity that seventy per cent of the women in this series had been delivered of one or more children. In this group, there were 20 who gave a history of one or more abortions, and six admitted one or more criminal abortions. There was a history of one previous ectopic gestation in the series. Eleven of the women had had previous pelvic operations. A definite history of previous pelvic infection was noted in eight other records. This is probably a lower incidence of pelvic infection than is actually correct, for histories were not obtained in all cases, and in some, the review may have been sketchy due to the emergency of the admission.

Amenorrhea.—That a history of amenorrhea is not always present, is witnessed by finding seventeen women in this series who had not missed a period. A fatal ectopic pregnancy occurred in a lactating woman. Thirty-eight women had missed one menstrual period, twenty-four had missed two periods, twelve had missed three or more. No history was available in nine women. Possibly one-third of this series might have been saved if they had sought adequate medical care, and had had pelvic examinations, at least, at the time of the second missed menstrual period.

Symptoms.—Vaginal bleeding and pain were almost equally distributed as initial symptoms. After the appearance of such symptoms, there was an excessive delay on the part of the woman in seeking medical aid in 58 per cent. Forty-two per cent sought medical advice within twenty-four hours of the initial symptom, seventeen per cent in 12 hours or less, twenty-five per cent within 12 to 24 hours. It is significant that these two symptoms, especially when associated with amenorrhea during childbearing period, are regarded so lightly by the laity. In all health instruction to women the gravity of this group of symptoms should be stressed.

Diagnosis.—The history was sufficiently typical in 13 cases that a diagnosis of ectopic pregnancy was made on it alone. In twelve cases, the diagnosis was made on pelvic findings, while in 19 cases diagnosis was based on both history and pelvic findings. In but one instance was a biologic test for pregnancy made. This was in a woman acutely ill with thyroid disease. Thus, in nearly half the cases a correct diagnosis was made before operation.

In twenty-one cases the true nature of the lesion was not accurately determined until operation. The incorrect diagnoses include six cases diagnosed as pelvic abscess or inflammatory disease, three as threatened or incomplete abortion, three as myoma, two as ovarian cyst and one each as acute appendicitis, acute abdomen, intestinal obstruction, uterine rupture and uterine perforation from intrauterine contraceptive stem pessary. In two cases laparotomy was performed because shock developed during observation. In six of these cases, the history was typical and each woman had a pelvic examination. Six of the women were not examined, and four gave a misleading history. In the remainder the histories were suggestive and pelvic examinations were made.

Diagnosis was not made until autopsy in 36 cases. Four cases were not operated on although the diagnosis was suspected in two who were badly shocked on admission, and in two cases where pneumonia was present and was judged to preclude operation. Most of these cases represent women not seen by a physician, or who refused hospitalization, or where the first attendant missed the diagnosis. Sixteen of these had typical or suggestive histories. Only twelve had pelvic examinations. A diagnosis of abortion was made in 6, pelvic inflammatory disease in five, and one each, tuberculous peritonitis, intestinal obstruction, anemia, benign uterine bleeding and retroversion.

Although many of these women gave strongly suggestive histories or had pelvic examinations, the index of suspicion of ectopic gestation was not high enough to lead the medical attendants to a correct diagnosis. Where pelvic examination was not made, the omission was almost equally due to the patient not seeking medical care until shock was present, or to an unexplained oversight on the part of the family physician or member of the hospital staff. In a few cases, an incorrect diagnosis led to omitting the pelvic examination.

Hospitalization.—It is relevant to this analysis to determine the interval from the first medical advice to hospitalization. It is on record that eighty-two women were seen at their homes by physicians. Of these, seven did not enter hospitals. In the others, it was recognized that hospitalization was necessary and 54, or 72 per cent, were referred for admission within 24 hours. Yet, in only 9 instances was the situation regarded as sufficiently serious that admission was obtained within six hours. Twenty-one cases were admitted to hospitals later than 24 hours after first being seen by a physician. Of these, 15 were not referred for 7 days or longer. Six women applied for hospital admission on their own initiative. The records of the remaining cases were unsatisfactory on this point.

It must be apparent that the true state of the condition for which medical aid was sought, and its acute emergency nature was largely overlooked by the family physician who first saw these cases.

Of the twelve women who were not admitted to a hospital, seven were seen by a physician. In five, the diagnosis was completely missed. In

two cases, medical advice as to hospitalization was refused. Five patients had no medical care whatever, and were reported to the Committee after autopsy by the staff of the Coroner's office.

Time of Operation.—There were 25 women admitted to the hospital who were not operated on. Two patients died immediately after admission, another was too greatly shocked and died within an hour, two had pneumonia. In nine, no diagnosis was made and the patients died while under observation. In eleven other cases, a presumptive, albeit incorrect, diagnosis was made. In four cases the condition was diagnosed septic abortion, in four pelvic inflammatory diseases, and one each as tuberculous peritonitis anemia, and retroversion.

Eighteen of the women admitted to hospital were not operated on until more than 24 hours after admission. Four were correctly diagnosed, while four were regarded on admission as abortion, threatened, or incomplete, three as myoma, two as pelvic abscess, and one each as thyroid disease, anemia, intestinal obstruction, ovarian cyst and shock. The last case was actively treated during this preoperative period.

In fourteen women the operation was delayed until within the second twelve hours after admission. One was regarded on admission as acute appendicitis, two as fibroids, fourth as an uterine hemorrhage. This patient had a cauterization of the cervix as a preliminary to an elective hysterectomy proposed for four days later. In three cases admitted at night, the operations were held up for elective surgery by the attending chief the following morning. In the remainder, the appearance of pronounced shock prompted a correct diagnosis.

In twelve cases, operations were performed more than two hours after admission, but, under 12 hours. In four instances, operation was delayed to treat evident shock, in the other eight, there was a delay in naming a correct diagnosis.

Twenty-one women were operated on within two hours after admission. On thirteen of the records it was stated that the patients were in shock. Only six of these patients were transfused. Two had transfusions during operation, four postoperatively and two had both types. The deaths in this group were ascribed to hemorrhage and shock in thirteen, peritonitis in four, embolus in two, intestinal obstruction in one and transfusion reaction in one.

It is evident that error or delay in making correct diagnosis was responsible for death of a large proportion of the women who were operated upon.

Operative Risk.—Twenty-one women, of the 65 operated on, were considered good operable risks. This decision was either stated on the hospital record, or has been based on the record of a normal blood pressure associated with a hemoglobin and erythrocyte count that did not reflect a marked degree of hemorrhage. Death was found to have occurred from peritonitis ten times. In eight of the infection deaths multiple operations had been performed, these included five appendectomies. In the remainder, the conclusion was drawn that an error in technique had occurred. Five women died from hemorrhage. In four cases there was either too much surgery or inadequate surgery, the fifth probably died of secondary hemorrhage. Three women died of pulmonary embolus, in one case the convalescence had been afebrile, in the other two a suspicion of infection had to be entertained. Three patients died of medical complications.

Nine women were operated on in whom the risk was regarded as fair by the attending surgeon, or could be so designated by the clinical and laboratory findings on the record. Three women died of infection. Multiple or inadequate surgery was regarded as causative in two of these cases. Five patients died of hemorrhage. Three of these had multiple operations or inadequate surgery. One patient died of a pre-existing renal infection.

Thirty-five women were operated on in shock. The paucity of transfusions during operation and immediately afterward undoubtedly accelerated the fatal termination. There were 26 deaths from hemorrhage. Prolongation of hemorrhage was caused seven times by delay of patient in seeking medical aid, or refusing hospitalization, or giving a misleading history. In sixteen cases the delay was evidently the fault of the family physician, or of the hospital staff in diagnosis, or in inexplicable delay in operating, or performing inadequate or multiple surgery.

Where operation was prompt and transfusions given during and after operation, the deaths were regarded as nonpreventable. One patient died of a transfusion reaction, another of hemiplegia and a renal shut-down. Seven women survived operation in shock to die later of infection. In all instances this was regarded as due to an error in technique.

Time of Death After Operation.—The efficiency of surgical and related therapy as well as the patient's capacity and ability to withstand hemorrhage, surgery and present or introduced infection is reflected in the length of time these women survived operation.

So we find three women died during operation, and nineteen women died within twenty-four hours after operation, all of shock and hemorrhage. Eleven of these deaths occurred within six hours. Only three of these patients received transfusions.

Seven women died in the second twenty-four hours after operation, three of shock and hemorrhage, four of infection, peritonitis. Only one transfusion was recorded in this group. In one woman, pneumonia was present in addition to the fatal peritonitis.

During the third, fourth, fifth and six days after operation the deaths numbered 18, of these, seven were due to hemorrhage, seven to infection, and four died as a result of the following added complications: transfusion reaction, left hemiplegia, and renal cortical necrosis, thyrotoxicosis, and congestive heart failure in a patient with known rheumatic heart disease.

On the seventh postoperative day, 18 deaths occurred. Twelve were deaths from infection, two from secondary hemorrhage, and four from added complications, one kidney lesion and three pulmonary emboli or infarcts, in two of which the postoperative convalescence had been afebrile.

Multiple Operations.—Among the deaths, there were 18 cases in which multiple operations were performed. These ranged upward to a series, in one woman, of dilatation and curettage, tracheorrhaphy, hemorhoidectomy, multiple myomectomy and bilateral salping-oophorectomy. The preoperative diagnosis here included possibility of bilateral ectopic pregnancy.

In nine cases where plastic operations or herniorrhaphies were done before the abdomen was opened, ectopic gestation had been diagnosed three times.

In ten cases, in addition to excising the affected tube, such other operations within the peritoneal cavity as appendectomy, myomectomy,

hysterectomy, defundectomy, suspension of the uterus and removal of the opposite tube and ovary were performed. It is noteworthy that in four of the five cases where the appendix was removed, death was caused by infection.

In the majority of these instances, the decision of the Committee assigning responsibility to the operating surgeon was based upon error in judgment in the performance of what was regarded as nonessential surgery in the presence of an acutely life-threatening situation, in addition to failure in diagnoses.

Incomplete Operations.—In addition to the five operations performed on ruptured cornual pregnancies, which were largely regarded by the Committee as inadequate surgery, there were eight cases in which the surgical treatment was considered incomplete. Four times this opinion was based upon the performance of a curettage or colpotomy, singly or combined without further treatment of the intraperitoneal lesion. In another instance, a two months' fetus was removed from the cul-de-sac and the pelvis drained. Again, the bleeding point on a tube was ligated, the tube not removed. In another the excised tube was reported by the pathologist not to have been the site of a pregnancy. In one case the tube was ligated on both sides of a perforation, the tube was not removed.

In the entire group the attending surgeon was regarded as responsible by the Committee, the avoidable factor being error in judgment.

Cornual Pregnancies.—There were eight deaths from cornual pregnancies in the series, five occurred in multiparas. In five, the pregnancy was advanced to the third month. Three died unoperated upon, two because of extreme shock, one because a receiving ward intern missed the diagnosis and the patient died after being sent home. In this instance, the enlarged tender cornua had been noted in prenatal clinic and diagnosed as subserous myoma.

In the five operations the cornual rupture was closed by suture; with removal of the adjacent tube and ovary in two, and with wedge shaped resection of the cornua in one case. The latter was the only one in which death did not occur within 24 hours. In this instance the patient, transfused during and after operation, developed sepsis. Some of these deaths might have been prevented had hysterectomy been performed.

Secondary Abdominal Pregnancies.—There were five deaths in which the ectopic gestations were secondary abdominal pregnancies.

In one the diagnosis was made by chance in a woman dying of pneumonia. At death, an immediate abdominal incision was made preparatory to a postmortem cesarean section. The fetus, dead and slightly macerated, but 7½ months' development, was found in a sac originating between the layers of the broad ligament. The patient had had constant prenatal care during her pregnancy.

In the second case, a primigravida with no prenatal care or examination, shock developed at the fourth month. At delayed operation, with the patient septic, the fetus was removed and the placenta left in situ on the broad ligament with packing and drainage. Septic death occurred on the third postoperative day.

The third case gave a history of missed abortion two years previously. There had been many pelvic examinations; with a diagnosis of multiple myoma, a hysterectomy was scheduled. A right broad ligament pregnancy with a six months' lithopedion was found and pelvic débridement performed. Death from secondary hemorrhage occurred on the fifth postoperative day.

The fourth case was under prenatal care until the eighth month. Abdominal pain was regarded as due to a ruptured uterus. Operation in shock revealed a secondary abdominal pregnancy, with death following on the operating table.

The fifth case was a three months' pregnancy attached to the sigmoid and parietal peritoneum. Patient had no previous care, was admitted in shock and promptly operated on. Transfusion was followed by acute hemolytic reaction, anuria and death.

Attempted Abortion.—Attempts at illegal interruption of pregnancy had been made in ten of the cases in this series, nine times by the patient and once by a physician. Misleading histories were the rule. Operation was performed in six cases. In two, however, the true diagnosis was revealed by laparotomy, subsequent to colpotomy done for suspected pelvic abscess. In the other four operative cases, shock and pelvic findings made operation imperative. Four of these women died of infection, six of shock and hemorrhage.

In each instance, because of the delay in seeking medical assistance after pregnancy was suspected, and after symptoms of both hemorrhage and infection were experienced, but also for the misleading history, the responsibility for the death was ascribed to the patient.

Transfusion.—Blood transfusions were given to only thirty-seven women. They may be principally grouped as six, preoperative; twelve during operation and nineteen postoperative.

In the group of six patients who had preoperative transfusions, the procedure repeated in the postoperative period in three, with one also receiving a transfusion during operation. The three patients who had only preoperative transfusion lived long enough for additional support to have been given later.

Transfusions were given during operation to 12 women; of this group one received in addition a pre- and a postoperative transfusion. Two of these were autotransfusions. One of these transfusions was followed by hemolytic reaction proved at autopsy.

Transfusions were given to 19 women 23 times in the postoperative period. Sixteen women were transfused only in this period. Only four patients received more than one transfusion. The time interval in the majority of cases was sufficient to have allowed more transfusions.

It is significant to note that in a group of women sick enough to die in most cases from hemorrhage or infection, that only slightly more than one-third were given transfusions.

Autopsy.—The regulations of the Coroner's office regarding sudden death at home or death within 24 hours after admission to the hospital, helped to produce the high incidence of 69 autopsies in this series of 101 deaths, and served to bring additional light upon many cases.

Causes of Death.—As might be expected, hemorrhage and shock caused the largest number of deaths—68. In three additional cases where hemorrhage was the principal cause peritonitis was also present.

In nineteen cases infection was the cause of death. One patient not operated on because of misleading history of attempted criminal abortion, died of infection.

Complications caused death in ten cases. There were three deaths from pulmonary embolus. Autopsy findings in each, two cerebral vascular accidents, these may have been embolic deaths, one each thyrocardiac, pneumonia, pyelitis and transfusion reaction.

Responsibility and Preventability.—In these as in all other puerperal deaths in Philadelphia since January 1, 1931, an attempt has been made

to determine the responsibility for and the preventability of the death, and the decisions of the Committee on Maternal Welfare of the Philadelphia County Medical Society are given here.

In eighteen deaths, the patients were regarded as responsible. In five additional cases, the responsibility was divided between the patients and a physician.

In thirteen deaths, the responsibility was assigned to one or more referring physicians, in most instances her family doctor, although one woman was misdiagnosed by four separate physicians. In seven additional cases, the responsibility was divided between the referring physician and the chief of the hospital division whose service received the patient.

In forty-five deaths, the responsibility was assigned to the hospital chief alone.

The thirteen deaths regarded as nonpreventable were so assigned where the patient died in spite of prompt recognition of the lesion and adequate surgery with transfusions, or where complications of a medical nature were the cause of death.

The eighteen deaths where the responsibility was assigned to the patients had the following factors: attempts at criminal abortion and misleading history, refusal of hospitalization or delay in seeking medical care.

In the joint responsibility of patient and physician, the factors on the patient's side were delay in medical care and attempt at criminal abortion and misleading history.

Where the referring physician was held responsible, the following factors were found: failure in diagnosis, delay in referring patient to hospital after correct diagnosis was made.

Where the referring physician was joined in responsibility with patient or hospital chief, his fault was entirely in the failure to make a correct diagnosis.

In the 45 deaths where the responsibility was assigned to the hospital chief and in those where he was held jointly responsible, the avoidable factors were error in judgment, with such underlying factors as failure in diagnosis, unexplained delay in operation, multiple surgery, inadequate surgery, no operation, and failure of continued treatment of shock after operation, chiefly lack of transfusion.

Error in technique was regarded as the avoidable factor in 10 cases of infection or secondary hemorrhage. In the whole group where the hospital chief was regarded as responsible for the death, there was a total of 15 deaths from infection.

Summary

This study presents a review of 101 fatalities from ectopic pregnancy occurring among the cases on record in Philadelphia from 1931 to 1943. It represents an attempt to fix responsibility for the death, and to seek out the avoidable factors.

The responsibility has been found to be divided between the patient and her family, the referring physician, and the attending surgeon and his hospital staff. The avoidable factors have been found to include lack of education of laity regarding early and adequate prenatal care; failure of referring physician in recognizing the possibilities of dif-

ferential diagnosis; failure on part of surgeon in diagnosis, delay in operating, lack of transfusion, and poor choice of operative procedure.

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Discussion

DR. JAMES R. MILLER, Hartford, Conn.—To the thorough critical review presented by Dr. Williams, I wish to add a survey of ectopic pregnancy in connection with maternal mortality records in Hartford, Connecticut. The first 20 years of the survey are those which I have previously studied and reported, and it so happens that they represent the period immediately preceding the first use of transfusion in the city (i.e., 1929), in the treatment of ectopic pregnancy.

The figures are as follows:

| | 1909 TO 1928 | 1929 TO 1944 |
|---|--------------|--------------|
| 1. Live births | 62,913 | 69,704 |
| 2. All puerperal deaths | 460 | 192 |
| 3. Maternal mortality | 0.7% | 0.27% |
| 4. Ectopic pregnancies | 565 | 357 |
| 5. Ectopic deaths | 23 | 8 |
| 6. Fatality percentage | 4.8% | 2.4% |
| 7. Ratio of ectopic deaths to all maternal deaths | 4% | 4% |

It is further interesting to record that since 1929, St. Francis Hospital reports no deaths in the last 141 cases, and the Hartford Hospital reports only 2 deaths in 184 cases, which gives a combined fatality rate of 0.6 per cent. Neither of the 2 deaths was caused by blood loss, for one succumbed to a typical transfusion (Rh?) reaction after her fourth transfusion, and the other died on the thirty-second postoperative day after repeated pulmonary emboli.

Two sets of factors have brought about this improvement, perhaps the same factors which have operated to reduce maternal mortality in such a spectacular and as yet unexplained fashion. These are: first, earlier diagnosis, earlier hospitalization and earlier consultation with "ectopic minded" specialists, and, second, the rapid replacement of blood loss, appropriate anesthesia, and restriction of operating privileges to those who are qualified. It is evident that a low fatality rate is a measure of the excellence of diagnosis among those practitioners who first see the patients, and to an equal extent, of the excellence of special skill available in the community's hospitals.

It is interesting to speculate on the causes of high or low incidence of ectopic pregnancy. If the important etiological factor is previous salpingitis, we may say that we have been having less salpingitis or have been treating it better than we did two or three decades ago.

DR. FRANK E. WHITACRE, New Orleans, La. (By invitation).—The difficulties in the diagnosis of ectopic pregnancy are well known. It is significant that, in the many reviews in the literature the number of patients operated upon for ectopic pregnancy is carefully analyzed, but rarely is there a mention made of the number of patients operated upon with a mistaken diagnosis of ectopic pregnancy.

Time does not permit a review of the etiology, but in general, any condition which obstructs the passage of the ovum from the ovary to the uterus, whether it be obstruction of the lumen from within or pressure on the tube from without, may produce ectopic pregnancy. In China, where the treatment of pelvic and abdominal tumors is neglected, and where pelvic inflammatory disease is common, it is natural that ectopic pregnancy is prevalent. At the Peiping Union Medical College, 56 ectopic pregnancies were seen between the years 1935 and 1940. An analysis of these accidents is in the process of preparation.

There are three types of cases which present themselves for diagnosis: First, those seen before rupture of the tube or tubal abortion has occurred; second, those

seen during the process of rupture or immediately thereafter; third, those cases seen days or weeks after the accident has occurred. The problems of diagnosis in the first two groups are well established, and it is in regard to the third group of cases that I wish to comment.

In this group, difficulties in diagnosis and treatment arise, for it is well known that pelvic inflammatory disease can produce the same symptoms. We will not review the methods of colpotomy or cul-de-sac puncture, which we still use, but call your attention to a further aid in the diagnosis of obscure cases. We have not been able to find reference in the literature to the use of spectroscopic examination of the blood serum for hematin as an aid in the diagnosis of ectopic pregnancy, although the detection of urobilinogen and the icterus index have been mentioned by Albert Mathieu. We believe that this test is of special value in determining the presence of extravasation of blood and the process of its absorption, as in ruptured ectopic pregnancy, either recent or remote.

Hemoglobin from the blood consists of globin and hematin. Blood coming into the peritoneal cavity decomposes to form hematin, which is absorbed in the blood stream and is detectable within a few hours. Hematin itself gives a weak spectrum. However, with the addition of ammonium sulfide it is reduced to hemochromogen, which possesses a good spectrum, with characteristic and typical bands, a narrow dark band at 5,580, and a faint wide band at 5,270. The test is simple, and a few c.c. of blood drawn from the arm vein can be tested in ten minutes. The technique is described in any standard text dealing with the spectroscope. Even the aspirated blood from cul-de-sac puncture can also be thus examined, and thereby rule out the possibility of confusion caused by the rare entrance of the aspirating needle into an anomalous vein. In the presence of a history and physical findings suggesting ectopic pregnancy, a positive spectroscopic reaction for hematin in the blood serum practically clinches the diagnosis. It is clear that any condition causing extensive hemolysis could give a positive reaction. Therefore, malaria and other hemolytic conditions must be ruled out. It is possible that a hemolytic streptococcus may be the cause of pelvic inflammatory conditions, but even then a positive spectroscopic test is not to be expected unless septicemia is present.

This test is suggested only as an aid in the diagnosis of some obscure cases, and without any thought that it could or should displace the well-known and reliable clinical methods. In our 56 cases, we have used this test only twelve times, and in these instances, it was always reliable. We feel that the test has helped us differentiate between pelvic hematoma and pelvic abscess, and has, therefore, aided us in avoiding doing a laparotomy in the presence of a pelvic abscess, which is usually better drained from below.

DR. LEWIS C. SCHEFFEY, Philadelphia, Pa.—I wish merely to emphasize that there has been a persistent and continuous improvement both in diagnosis and treatment of ectopic pregnancy. At the Jefferson Medical College Hospital, out of 82 patients seen on the ward service from 1921 to 1931, there were 4 deaths, a total mortality of 4.8 per cent. Two of these patients died before being taken to the operating room. The remaining two deaths gave an operative mortality of 2.5 per cent, and one of these patients dying from infection following an autotransfusion, the other as the result of delayed diagnosis. There were 75 admissions from 1931 to 1942, with only one death. This shows a reduction of total and operative mortality to 1.3 per cent, with an operative mortality for the combined series of 1.9 per cent. The combined total mortality was 3.2 per cent. I attribute the improvement in the second decade, as emphasized by both Dr. Williams and Dr. Miller, to the well-known improvement in methods of supportive treatment.

SODIUM PENTOTHAL ANESTHESIA IN OBSTETRICS*

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BETWEEN September 1, 1940, and March 31, 1944, 1,415 deliveries were carried out at the Johns Hopkins Hospital under sodium pentothal anesthesia. Both 2.5 and 5 per cent solutions of the drug were used, but since the latter concentration has proved more satisfactory in our hands, this has been employed in the great majority of the cases. The amount of sodium pentothal necessary for a low forceps delivery together with episiotomy and repair, lies between 0.75 and 1.0 Gm. (from 15 to 20 c.c. of a 5 per cent solution) provided that some form of sedation has been administered in labor such as barbiturates or paraldehyde; in cases in which sedative drugs have not been administered, a somewhat larger dosage of sodium pentothal may be necessary. For cesarean section 1.5 Gm. (30 c.c. of a 5 per cent solution) is the quantity usually required. The amount is never allowed to exceed 2 grams. Except in cases in which scopolamine has been given, atropine (0.5 mg., or $\frac{1}{130}$ gr.) is routine. During the past year, oxygen has been administered prior to the birth of the baby as a prophylaxis, possibly unnecessary, against fetal anoxia. In the majority of the cases reported, either a barbiturate plus scopolamine, or paraldehyde, had been previously administered to amnesic levels and usually such patients were under the full effects of these drugs at the time the sodium pentothal anesthesia was started. Over 90 per cent of the anesthetics were given by members of the house staff, the remainder by professional nurse anesthetists.

Our impression of sodium pentothal anesthesia in general, is in keeping with the many favorable reports which have issued from various surgical clinics. Induction is instantaneous and quiet. The patient is unconscious within twenty or thirty seconds after the first few c.c. of the solution enter the vein, and actual operating can usually be started within a minute or so—this without “pushing” the anesthesia. Postoperative vomiting is rare and there is little “hang-over.” There were but three cases of postoperative pneumonia in the 1,415 cases. In our experience, moreover, patients much prefer sodium pentothal to other types of anesthesia they have had.

As may be seen in Table I, the majority of the cases under consideration represented operative deliveries (68.1 per cent), but a suffi-

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TABLE I. ANALYSIS OF 1,415 DELIVERIES UNDER SODIUM PENTOTHAL ANESTHESIA ACCORDING TO TYPE (SPONTANEOUS OR OPERATIVE), PARITY AND INCIDENCE OF PREMATURITY

| | | | |
|----------------------|-------------|-----------------------|-------------|
| Spontaneous | 452 (31.9%) | Operative | 963 (68.1%) |
| Primiparas 144 | | Primiparas 713 | |
| Multiparas 308 | | Multiparas 250 | |
| Premature 50 (11.1%) | | Premature 124 (12.9%) | |

cient number of spontaneous deliveries (452) were managed under sodium pentothal anesthesia to permit of certain general conclusions. In employing this agent for spontaneous delivery, it was our hope to administer it à la reine toward the end of the second stage, deepening the anesthesia with pains and allowing the patient to regain semiconsciousness between. This proved unsuccessful for two reasons: (1) The procedure entailed dealing for the most part with semi-anesthetized patients and it is well known, of course, that this state of partial anesthesia is associated with particular dangers; (2) since the patient, semiconscious, often moved about under the stimulation of pains, the needle frequently became dislodged from the vein giving rise to serious mechanical difficulties. It is our opinion, accordingly, that sodium pentothal anesthesia is not suitable for spontaneous delivery.

TABLE II. ANALYSIS OF 963 OPERATIVE DELIVERIES UNDER SODIUM PENTOTHAL ANESTHESIA ACCORDING TO TYPE OF OPERATION

| | |
|------------------------|-------------|
| Low forceps | 777 (80.7%) |
| Cesarean section | 114 (11.8%) |
| Breech extraction | 51 (5.3%) |
| Version and extraction | 15 |
| Craniotomy | 3 |
| Midforceps | 3 |

The types of the 963 operative deliveries performed under sodium pentothal anesthesia are shown in Table II. The great majority, of course, were low forceps, and for this procedure this form of anesthesia has rapidly become routine in our clinic. Although the relaxation of the abdominal walls provided by sodium pentothal is not sufficient for many abdominal operations, it is quite adequate for cesarean section. Bleeding is less than with gas-oxygen-ether, as is also, in our opinion, postoperative distention. Of the fifteen versions and extractions reported, six were on second twins, and in the remainder of cases, the babies were small. Except for versions on second twins, sodium pentothal is ordinarily contraindicated for this operation because the uterus does not relax well.

Before considering the fetal and maternal mortality rate in the present series, it is important to note, as shown in Table III, that sodium pentothal passes through the placenta, and within ten or twelve minutes, reaches equal concentrations in fetal and maternal bloods. However, there is a period of five minutes after starting the anesthesia during which the amount of drug reaching the fetus is very small and

TABLE III. MG./100 BLOOD ACID PENTOTHAL IN MOTHER AND CHILD AT DELIVERY

| GM. OF SODIUM PENTOTHAL GIVEN | DURATION OF ANESTHESIA | MOTHER MG./100 | INFANT MG./100 |
|----------------------------------|---------------------------|-------------------|-------------------|
| 0.7 Gm. | 5 minutes | 3.9 | 0.8 |
| 0.45 Gm. | 6 minutes | 2.5 | 1.4 |
| 0.35 Gm. | 7 minutes | 2.4 | 1.25 |
| 0.55 Gm. | 9 minutes | 3.0 | 1.75 |
| 0.40 Gm. | 12 minutes | 2.25 | 2.50 |
| 1.00 Gm. | 12 minutes | 6.2 | 5.0 |
| 0.55 Gm. | 15 minutes | 0.75 | 0.5 |

throughout the first ten minutes is decidedly less, as a rule, than after fifteen or twenty minutes of anesthesia. This fact should not be taken as an indication to hurry the delivery; however, it does afford an opportunity to spare the fetus an unnecessary quantity of the drug, that is, the start of the anesthesia should be postponed until everything is in immediate readiness for the operation. The method employed for the determination of sodium pentothal in the blood was developed by Hellman and Shettles and has been published elsewhere.

TABLE IV. STILLBIRTH AND NEONATAL MORTALITY (COMBINED) IN 1,421 INFANTS DELIVERED UNDER SODIUM PENTOTHAL ANESTHESIA

| | INFANTS | DEATHS | PER CENT |
|--|---------|--------|----------|
| Total infants | 1,421 | 70 | 4.9 |
| Fetal heart heard prior to anesthesia | 1,386 | 33 | 2.4 |

The stillbirth and neonatal mortality rates (combined) for the 1,421 infants born in this series are shown in Table IV. For the purposes of this study, the neonatal period includes the period of stay in the hospital up to and including the thirtieth day; the usual duration of stay was ten days. There were seventy cases in which the baby was lost, giving a total stillbirth and neonatal mortality rate, uncorrected, of 4.9 per cent. Among these seventy cases associated with fetal exitus, there were fifteen cases of premature separation of the placenta in which the fetal heart was not heard on admission to the hospital; there were three cases of prolapse of the umbilical cord, pulsations having stopped on admission; there were three cases of hydrocephalus necessitating craniotomy; four cases of fetal death in utero long before the onset of labor, and a number of other cases in which the fetal heart ceased for various reasons prior to the onset of the anesthesia. If we are to make an intelligent attempt to evaluate the possible effect of sodium pentothal on fetal prognosis, it would seem obligatory to eliminate from consideration these cases (thirty-seven in all), in which the fetus had clearly died before the anesthetic was started, or suffered craniotomy. If this subtraction be made, the resultant stillbirth and neonatal mortality rate becomes 2.4 per cent, that is, thirty-three infants lost among 1,384 infants, in all of which cases the fetal heart was audible when the anesthesia was started.

The causes of death in these thirty-three infants are listed in Table V. The ten premature infants all weighed less than 2,000 grams and showed at autopsy extensive atelectasis. The question may be raised,

TABLE V. CAUSES OF THIRTY-THREE INFANT DEATHS—IN ALL OF WHICH CASES THE FETAL HEART WAS AUDIBLE BEFORE ANESTHESIA WAS BEGUN

| DIAGNOSIS | INFANTS |
|---|----------|
| Prematurity | 12 |
| Intracranial hemorrhage | 8 |
| Congenital abnormality | 5 |
| Excessive size baby (5,320 Gm.); traumatic delivery | 1 |
| Meningitis—21 days post partum | 1 |
| Unknown | 4 |
| (Maternal diabetes 1; Face presentation 1; Breech presentation 1; Intrapartum infection 1) | |
| Asphyxia following placenta previa | 2 |
| | <hr/> 33 |

of course, as to whether the anesthesia may not have contributed to the pulmonary inadequacy. This possibility cannot be denied, but on the other hand, it may be stated that our prematurity mortality with sodium pentothal has been slightly less than with other forms of anesthesia. There were four cases, listed as "Unknown," in which the cause of death was not altogether clear, but in each of these cases, a pathological condition was present which could well have accounted for the infant's death. In order to inquire further into the effect of sodium pentothal anesthesia on stillbirth and neonatal mortality, we have compared the total infant loss in our series of operative deliveries done under sodium pentothal with a comparable number of operative deliveries performed under gas-oxygen-ether anesthesia. As may be seen in Table VI, the rates both in the two total series and in the two groups of full-term cases are practically identical. As far as we have been able to determine, there was no instance in the entire series of 1,415 cases delivered under sodium pentothal anesthesia in which this anesthetic agent was directly responsible for an infant's death, or in which it played any demonstrable role.

TABLE VI. STILLBIRTH AND NEONATAL MORTALITY RATES (COMBINED) IN 1,467 OPERATIVE CASES DELIVERED UNDER GAS-OXYGEN-ETHER ANESTHESIA (1937 TO 1939) AND IN 963 OPERATIVE CASES DELIVERED UNDER SODIUM PENTOTHAL (1940 TO 1944)

| | GAS-OXYGEN-ETHER | | | SODIUM PENTOTHAL | | |
|----------------|------------------|--------|----------|------------------|--------|----------|
| | CASES | DEATHS | PER CENT | CASES | DEATHS | PER CENT |
| Total | 1,467 | 88 | 6.0 | 963 | 55 | 5.8 |
| Full term only | 1,400 | 50 | 3.6 | 829 | 30 | 3.6 |

It is our impression that blood loss is less with sodium pentothal than with gas-oxygen-ether. The incidence of postpartum hemorrhage in the present series (600 c.c. or more) was 2.8 per cent.

There were two maternal deaths in the series as follows:

U. 251,366.—Registered, colored 19-year-old primigravida, E. D. C., 6/12/42; twin pregnancy. Eight visits to prenatal clinic. No deviations from normal until eighth visit, 5/28/42, when blood pressure was 150/100, albumin trace, weight gain 4 pounds in last week; slight edema, no symptoms. Admission to hospital, 11:00 A.M., 5/28/42.

During first eight hours in hospital blood pressure rose to 190/110; albumin 2+; headache, vomiting, epigastric pain. Paraldehyde 20 c.c. every 4 hours, per rectum.

Twenty-five hours after admission (12 noon, 5/29/42), blood pressure 170/110. Cervix 1 cm. dilated; half effaced; head at spines. Membranes stripped back and *ruptured artificially* (12:30 P.M., 5/29/42).

Latent period, 3 hours. Marked uterine inertia with 29-hour first stage, blood pressure remaining 170/110, albumin 4+. Restlessness changed to apathy, then to semicoma; anuria developed; then generalized convulsion at 6:00 P.M., 5/30/42 (30 hours after induction).

Following convulsion, blood pressure fell to 110/70; pulse 160 to 170 with picture of collapse; semicoma. After 2½-hour second stage, delivery under sodium pentothal anesthesia of stillborn, macerated twins at 10:50 P.M., 5/30/42. Only 0.5 Gm. of sodium pentothal was used. Despite transfusion with whole blood and plasma, blood pressure fell. Marked edema of lungs; temperature 104.3° F.; pulse 170.

Death occurred 6:48 A.M., 5/31/42, eight hours post partum; no autopsy.

U. 287,822.—Colored 16-year-old primigravida at term, referred from Calvert County, Maryland. Blood pressure 190/130; albumin 10 grams per liter; history of 74 pounds weight gain in pregnancy; massive edema, eyes nearly swollen shut and edema of thighs so marked as to interfere with rectal examination; nearly blind; headache, epigastric pain and vomiting for 3 days.

After 4 hours of observation and sedation, cesarean section done at 11:30 P.M., 3/29/43. While anesthesia was being induced with sodium pentothal, and after 0.75 Gm. had been given, the patient suffered either an atypical convulsion or laryngospasm. The sodium pentothal was stopped, and drop ether given for the entire duration of the operation.

After operation, persisting coma and edema of lungs. Blood pressure 175/95 but fell progressively.

Death at 11:35 A.M., 3/30/43 with picture of overwhelming edema of lungs.

Autopsy showed extreme edema of lungs; eclamptic liver.

In regard to the first of these deaths, the condition of the patient was becoming progressively worse for several hours prior to delivery and continued downhill at about the same rate post partum. There was no evidence that the anesthetic aggravated the patient's condition. Although the second case must be classified as an anesthetic death, it can be charged against ether with as much justification as against sodium pentothal, and can be charged with even greater validity to poor clinical judgment on our part. On retrospect the extraordinary fulminancè of the toxemia process, long neglected, made cesarean section under any form of anesthesia hazardous and, in our opinion, it was probably this step rather than the sodium pentothal used for induction which was the deciding factor in the fatal outcome.

In addition to the 1,415 cases herewith reported in which sodium pentothal anesthesia was used for delivery, we have employed this anesthetic agent successfully in approximately 500 additional obstetric operations not intended for immediate delivery of an infant—notably in puerperal tubal ligation, completion of incomplete abortion, artificial rupture of the membranes for the induction of labor, and manual removal of the placenta.

In conclusion, it is not the purpose of this paper to claim that sodium pentothal is an ideal anesthetic for operative obstetrics nor even that it is the best—certainly not for all cases. As our figures indicate, however, we have found it satisfactory in a substantial series of cases, are using it almost routinely for low forceps and cesarean sections, and believe that it constitutes an important addition to obstetric anesthesia.

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Hellman, L. M., Shettles, L. B., and Stran, Herbert: A Quantitative Method for the Determination of Sodium Pentothal in Blood, *J. Biol. Chem.* 148: 293-297, 1943.

Discussion

DR. THADDEUS L. MONTGOMERY, PHILADELPHIA, PA.—Reports upon the use of intravenous anesthesia in obstetric practice have appeared from time to time in the medical literature of recent years (Rucker,¹ Kassebohm and Schreiber,² Solomons,³ La Breeque,⁴ Hunt and Lundy⁵). None of them compares in size or scope with the series which Dr. Eastman has presented this morning, and none comes so close to telling what is the place of this newer anesthetic agent in obstetric practice.

The author's statement that "it is not the purpose of this paper to claim that sodium pentothal is an ideal anesthetic for operative obstetrics, nor even the best," but that "we have found it satisfactory in a substantial series of cases" is a measured expression of opinion in a field where overstatement is so often the rule.

If I had any criticism to offer, it would be with his failure to point out some of the dangers and the contraindications of the method. Some of these situations may be surmised from the content of the paper, others are so well recognized in surgical practice that they certainly must apply to obstetric procedure as well.

In view of the fact that pentothal is eliminated through the liver and may add to degenerative changes in that organ, one should be cautious in employing this drug in pre-eclampsia, just as he would in administering chloroform. Wherever there is already respiratory depression, a tendency to pulmonary edema, and faulty exchange of oxygen and carbon dioxide—as exists in advanced pre-eclampsia—one would be additionally hesitant to employ an agent that has known respiratory depressant effects. Its use therefore, in the two toxemic patients who died seemed to me unwise, although it may not have precipitated the fatal issue.

Since it is known that pentothal is rapidly conveyed across the placental barrier to the fetal blood stream, and since it has been demonstrated by Dreisback and Snyder⁶ that intravenous pentothal reduces the respiratory activity of the intra-uterine animal to a level below one-third, it seems unwise to employ this agent in cases of prematurity, for fear of inhibiting the initial respiratory effort in the newborn infant.

In the presence of active or of potential hemorrhage, most of us are loath to employ intravenous anesthesia. Personally, I have seen one or two disturbing reactions when it was given for the evacuation of freely bleeding incomplete abortions. We have abandoned its usage in such cases, preferring cyclopropane. Wood and

Jaco⁷ find a 24 per cent reduction in the lethal dose of pentobarbitone after hemorrhage of 20 c.c./kg. in rabbits, and Bernstein and Hershey⁸ point out on the basis of their clinical and experimental observations the unpredictable effect of pentothal sodium on the circulatory system in the face of hemorrhage. For these reasons, one should be hesitant in employing pentothal in the presence of actual or potential obstetric hemorrhage.

Finally, Dr. Eastman states that these anesthetics were all administered by members of his resident staff or by nurse anesthetists. No doubt with the frequent experience acquired from such a large series of cases, his departmental personnel soon became competent to administer and supervise intravenous pentothal anesthesia. A word of caution is in order, however, for the obstetrician who conceives of employing this agent in the *occasional case*. This method is not without its intrinsic dangers, technical difficulties, and its own complications, as listed by Hunter,⁹ independent of the obstetric problems involved. The anesthesia cannot be supervised satisfactorily from the far end of an obstetric delivery table. It is better to call in a skilled anesthetist to handle the anesthesia while you tussle with the obstetric delivery.

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DR. M. PIERCE RUCKER, RICHMOND, VA.—Before the advent of pentothal sodium anesthesia, I had had considerable experience with evipal anesthesia in obstetrics at Brookfield. This is a home for unmarried girls and there is no anesthetist regularly in attendance. Under the circumstances, intravenous anesthesia with evipal soluble answered very well in most instances. A single measured dose according to the weight of the patient was given, gloves were changed, forceps applied, an episiotomy done, the baby delivered, and the perineum was repaired. If there was no hitch, the patient awakened just as the repair was finished. However, if the baby needed resuscitation some other anesthetic, such as local, was needed for the repair, but this was rarely necessary.

With this background, when sodium pentothal was shown to be a safe anesthetic in selected surgical cases, I had fewer misgivings about using it in obstetrics than I otherwise would have had. On the obstetrical service of the Johnston-Willis Hospital we have used pentothal sodium for 758 anesthetics. Ninety-eight of the cases on the obstetrical service did not involve a viable baby, the cases in which this type of anesthesia was used are tabulated on page 858.

There was no conscious selection of cases. In most instances, the patient was given some form of first stage sedation, usually sodium amytal and hyoscine with rectal ether or paraldehyde as indicated. In some of the more recent cases, demerol was used. In a few patients who went into labor prematurely, an effort was made

| | |
|----------------------------|----|
| Dilatation and curettage | 83 |
| Delivery of the placenta | 3 |
| Vaginal packing | 1 |
| Abdominal abortion | 1 |
| Vaginal salpingectomy | 1 |
| Incision of breast abscess | 1 |
| Abdominal hysterectomy | 3 |
| Cautery and minor surgery | 3 |
| Chorionepithelioma | 1 |

In 660 cases, a viable infant was involved. The types of delivery being as follows:

| | |
|--|-----------|
| Spontaneous delivery | 55 |
| Low forceps | 435 |
| Midforceps (including 3 Scanzoni applications) | 94 |
| Breech extractions | 26 |
| Version and extraction | 48 |
| Craniotomy | 1 |
| Low flap cesarean section | 1 |
| | <hr/> 660 |

to stop labor with morphine, and if this were unsuccessful, they were given hyoscine, paraldehyde, etc. When the presenting part is out of the cervix, it is our custom to give the patient an anesthetic and deliver her by whatever means seem to be the easiest in the particular case. Except where inhalation anesthesia is contraindicated, or where the patient has expressed a desire for a particular kind of anesthesia, the choice of the anesthetic is left to the intern. The interns change so rapidly now that I am unable to say what were their guiding principles, if any. Some interns like to give intravenous anesthesia and give it well. Others are somewhat indifferent and prefer to pour a little ether.

The first 100 cases of this series were reported by Dr. Edwin Rucker in 1942. He started using a 2.5 per cent solution, and I have seen no reason for changing. The maximum dose used was 1,500 mg., the minimum 175 mg., and the average was 625 milligrams. I have not exceeded the extremes mentioned above, but the average dose has been somewhat reduced. I rarely use now as much as a half gram. There have been no complications on the delivery table. Sometimes when the respirations become very shallow, we give the mother oxygen in order to prevent anoxia of the baby.

Of the 660 babies, eight died within two weeks. Five died intrapartum, and three were classed as antepartum deaths, two of the latter being macerated. This makes a gross fetal mortality of 2.42 per cent.

There were the following maternal complications:

| | |
|---------------------------------|----|
| Eclampsia | 1 |
| Pre-eclampsia | 6 |
| Ablatio placentae | 1 |
| Detachment of the retina | 1 |
| Placenta previa | 3 |
| Inertia | 6 |
| Constriction ring | 13 |
| Incarcerated placenta | 1 |
| Prolapsed arm | 2 |
| Prolapsed cord | 1 |
| Postpartum hemorrhage | 7 |
| Febrile puerperium | 38 |
| Phlebitis | 2 |
| Mastitis | 12 |
| Pyelitis | 14 |
| Cystitis | 4 |
| Urinary retention | 22 |
| Cholecystitis | 1 |
| Acute dilatation of the stomach | 1 |
| Hydramnion | 1 |
| Psychic disturbances | 5 |

There was one maternal death. No autopsy could be obtained in this case, but the symptoms were similar to those described by Steiner and Lushbaugh as being due to multiple emboli of the lungs. The patient was an 18-year-old primipara. Labor was induced at term by rupturing the membranes. After a latent period of five hours and twelve minutes and a labor of seventeen hours and thirty-nine minutes, the cervix was fully dilated. The head was in R.O.P. position. An easy version and extraction were done. The anesthetic consisted of sodium amytal, gr. vi, hyoscine gr. $\frac{5}{200}$, paraldehyde 3ii, rectal ether 3iiss, sodium pentothal 625 mg., and pudendal block with novocain. The baby, a girl, cried promptly and did well. One cubic centimeter of ergotrate was given the mother as soon as the aftercoming head was out of the cervix, and the intact placenta was delivered two minutes later. It was followed by a little trickle of blood such as we do not often see with the use of ergotrate intravenously. The cervix was inspected and was found unlacerated, and bleeding was easily controlled by elevation of the fundus with the hand on the abdomen. The patient regained consciousness before the episiotomy repair was completed. She was put to bed in apparently good condition with a blood pressure of 90/60. However, her respirations were 60, and her pulse was 200. This was attributed to the hyoscine that had been given her and the restlessness that it had induced. About one and three-quarter hours after delivery, her condition suddenly changed and she died two hours after delivery. A few minutes before she died, there was a moderate vaginal hemorrhage. As an indication that there was no selection of cases, I append the following list of accompanying diseases in these 758 patients.

| | |
|--|----|
| Upper respiratory infection | 24 |
| Severe asthma | 1 |
| Typhoid vaccination (antepartum) | 2 |
| Enteritis | 11 |
| Mucous colitis | 1 |
| Intestinal obstruction | 1 |
| Appendicitis | 2 |
| Exploratory operation | 1 |
| Mumps | 2 |
| Measles | 1 |
| Abscess of tooth | 4 |
| Corneal ulcer | 1 |
| Iritis | 1 |
| Food poisoning | 1 |
| Hernia | 2 |
| Peptic ulcer | 1 |
| Diabetes | 2 |
| Infectious arthritis | 2 |
| Acute nephritis | 1 |
| Chronic nephritis | 2 |
| Obesity | 24 |
| Chorionepithelioma | 1 |
| Hepatitis (after yellow fever vaccine) | 1 |
| Otosclerosis | 1 |
| Migraine | 3 |
| Epilepsy | 3 |
| Hay fever | 1 |
| Urticaria | 5 |
| Furunculosis | 1 |
| Scabies | 2 |

It is my considered opinion that sodium pentothal has a place among the obstetric anesthetics.

DR. RICHARD W. TE LINDE, BALTIMORE, MD.—As a supplement to Dr. Eastman's report on pentothal sodium in obstetrics, I would like to give you our experience with this anesthetic agent in the gynecological service at Johns Hopkins. From October, 1939, until March, 1944, we have used pentothal sodium as an an-

esthetic 4,643 times without a single death that could be attributed to the anesthetic. At first we used it only for minor procedures, and such are still our commonest indications, as a total of 3,920 of our 4,643 cases were minor ones. Pentothal sodium has greatly facilitated the work of a busy operating room because the induction period is so brief and the period of recovery short and pleasant.

Pentothal has helped us in the present hospital bed shortage, for we now rarely hospitalize a patient for a diagnostic curettage. She is instructed to come to the operating room at an appointed hour without breakfast. The heart and lungs are checked before the anesthesia is administered. Following the minor operative procedure, the patient is permitted to rest for several hours on a bed in a room on the operating room floor. Late in the afternoon she goes home in company with a friend. She is never permitted to drive her own car home. In carrying out this routine, we have had no complications after the patients have left the hospital.

We have gradually extended the use of pentothal sodium and have found it of great value in relatively short vaginal plastic operations, such as those which can be done in an hour. Often this hour of anesthesia can be obtained with 1.0 Gm. of pentothal sodium in combination with a 50/50 nitrous oxide-oxygen mixture. We have found it of special value in plastic operations on elderly people with prolapse and allied conditions when it is desirable to avoid ether anesthesia. Occasionally, we have used it with nitrous oxide and oxygen for longer major operations when other anesthetic agents were contraindicated, but we have made it a rule never to exceed a total dosage of 2.0 grams.

Finally, we are using pentothal sodium with increasing frequency for induction before ether anesthesia. By using 0.1 Gm. of nembutal or seconal for premedication and pentothal for induction, we have been able to obtain all the advantages of avertin basal anesthesia, without the disadvantages.

The only complication of any consequence which we have encountered is an occasional laryngospasm. Forced oxygen and artificial respirations have in each instance overcome this. It is important to insist upon an empty stomach, for vomiting may throw the larynx into spasm.

We use the drug only in 2.5 per cent solution. Since doing this, we have had no venous thromboses and the increased volume over the 5 per cent solution of itself insures a slower induction which is less apt to result in laryngospasm.

DR. EASTMAN (closing).—We began the use of pentothal sodium anesthesia with some trepidation but as we gained more confidence in it, we found that we were employing it in our most desperate cases. Our series contains a large number of cases of placenta previa and premature separation of the placenta. Although there may be theoretical objections to the drug in the cases associated with hemorrhage, we seem to have had very satisfactory results in this type of complication and are continuing to use it.

Dr. Montgomery's criticism of sodium pentothal anesthesia in severe toxemias of pregnancy is more valid, in my opinion, and in the light of our experience, we are inclined to question the wisdom of its use in severe pre-eclampsia. Of course, that would apply to any form of general anesthesia.

Special Article

REPORT OF FIRST 50 CASES OF THE OVARIAN TUMOR REGISTRY CONDUCTED BY THE AMERICAN GYNECOLOGICAL SOCIETY*

EMIL NOVAK, M.D., BALTIMORE, MD.

THE American Gynecological Society appointed, in 1942, from its Fellows a "Committee on Ovarian Tumors," whose function was to be the inauguration and conduct of an **American Registry of Ovarian Tumors**. The committee consists of Drs. Robert Meyer, George H. Gardner, Karl H. Martzloff, Herbert F. Traut, and the writer as chairman. The need for such a project seemed obvious. The great frequency and the clinical importance of ovarian neoplasms, the lack of knowledge concerning the histogenesis of most of these, the confusion and unsatisfactoriness of systems of classification and nomenclature, the uncertainties as to the prognosis in many tumor types, the increasing interest in certain rather newly recognized types and the inadequacy of our knowledge as to their pathological and clinical characteristics—all these considerations pointed to the need of some cooperative attempt to advance our knowledge in this important field.

It seemed clear that the keystone of such an undertaking, aside from the primary one of collecting suitable material in sufficiently large amount, must be to correlate authoritative pathological study with observations as to the clinical course of the tumors under study. As by-products of such an investigation one might hope that something could be learned as to the histogenesis of ovarian neoplasms, as well as to certain group characteristics, so that a more generally satisfactory system of nomenclature might ultimately be worked out for the guidance of both clinicians and pathologists. While it might be a good many years before a sufficiently large number of some of the relatively rare ovarian tumors could thus be accumulated, the Registry should sooner or later develop into a valuable storehouse of material which had been evaluated with reasonable authoritativeness, and this material could be made available for future investigators in this field.

The general plan of work of the committee need not be here reviewed, having been outlined in two announcements made in the *JOURNAL OF OBSTETRICS AND GYNECOLOGY* (September, 1943, and January, 1944), and one in the *Journal of the American Medical Association*. It is still far from perfect in its working, and improvements will undoubtedly have to be made. Some of these have been discussed in the formal report to be made at the business meeting of the Society. The collection of material for study has been in operation only since the first announcements were published, scarcely more than one and a half years ago, and during this time the committee has just about gotten the "feel" of its job. The number of cases thus far submitted to the committee is still relatively small, and one of the purposes of this preliminary paper is to imbue clinicians and pathologists with the importance of such a cooperative project.

*Presented at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

Another reason was the feeling that the Fellows of the sponsoring organization would be interested in hearing something as to the kind of material which has thus far been gathered, since it can be taken as an index of what might be expected in the future. This report is limited to the first 50 cases referred to the Registry, simply because that relatively small group permits of at least a very brief recording of each. In addition, a few of the more interesting cases, especially those in which the diagnosis has been doubtful, are described somewhat more fully, with photomicrographic illustration, and these may even possess some educational value.

As might be expected, and as is inevitable with any large amount of pathological material, a small proportion of cases was encountered in which the pathological diagnoses made by different members of the committee differed rather sharply and sometimes irreconcilably. Most of these are included in the illustrations accompanying this paper. On the other hand, in the overwhelming majority of the cases, there has been essential unanimity in the diagnoses submitted by the members of the committee. The occasional discordancy of a single member's diagnosis has been disregarded in the final classification.

As will be noted in reviewing the short case synopses of the fifty cases herein submitted, there have been not a few in which the clinical history has been very incomplete, sometimes through no fault of the contributor, and others in which the slides submitted were likewise far from satisfactory. For the present it has seemed best not to reject these cases from study, although it is possible that they may have to be winnowed out of the Registry later.

One of the most important parts of the committee's work will be the follow-up study of all Registry cases, and such data have been secured on most of the cases included in this report. Since many of these cases are very recent, and since the number of cases of any one tumor group is still very small, there would be no point in tabulating these follow-up studies in this early phase of the work. A brief note as to the present condition of the patients is, however, appended to each of the short case synopses, where such information has already been obtained.

Table I is a tabulation of this first group of 50 cases, and it shows the wide variety and the interesting character of the material which is being

TABLE I

| | |
|---|----|
| Primary adenocarcinoma | 1 |
| Secondary adenocarcinoma | 4 |
| Serous papillary cystadenocarcinoma | 4 |
| Granulosa cell carcinoma | 9 |
| Thecoma | 4 |
| Arrhenoblastoma | 1 |
| Dysgerminoma | 3 |
| Brenner tumor | 4 |
| Mesonephroma | 1 |
| Krukenberg tumor | 3 |
| Lymphosarcoma | 1 |
| Adrenal tumor | 2 |
| Fibroma | 2 |
| Pseudomucinous cystadenoma (with fibroma) | 1 |
| Serous cystadenoma | 1 |
| Endometrial cyst | 1 |
| Corpus luteum cyst | 1 |
| Doubtful | 7 |
| Total | 50 |

received. The committee is most grateful to the many physicians who have helped in this cooperative study by sending in material and supplying clinical and follow-up information. Below is given a very brief synopsis of each of the 50 cases on which this first report is based.

Case Reports

CASE 1.—(Dr. W. P. L. McBride, Rutland, Vt.) Tumor of right ovary in child 5 years of age. Preoperative diagnosis—acute appendicitis, but operation (July, 1942) disclosed friable infiltrated mass in region of right ovary, with numerous implants on peritoneum and adjacent bowel. Death soon after operation. Previous health good, with no abnormal sex characteristics.

Classification. Secondary adenocarcinoma of ovary (primary seat unknown). (Fig. 1.)

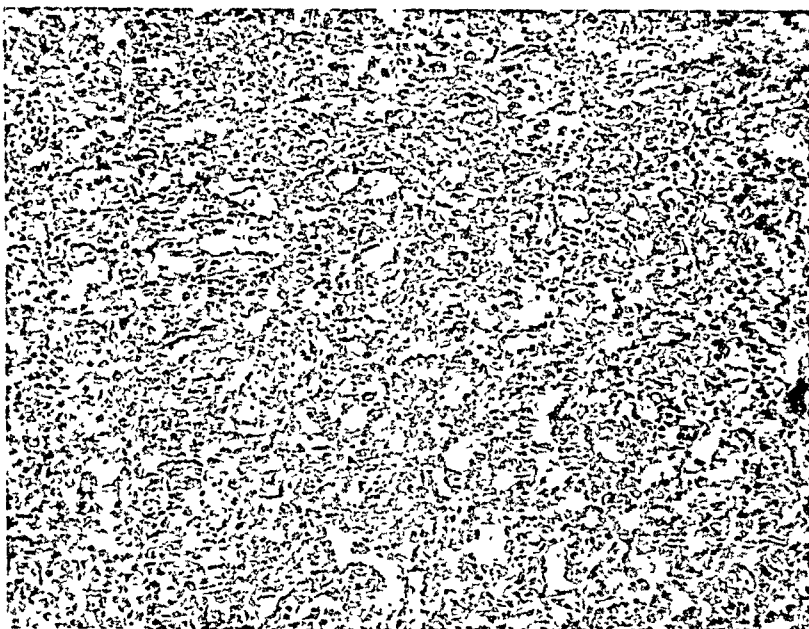


Fig. 1.—(Case 1.)

CASE 2.—(Dr. A. F. Liber, Amsterdam, N. Y.) A typical Brenner tumor (received Dec. 6, 1942) from a patient of 42.

Classification. Brenner tumor of ovary. (Fig. 2.)

Follow-up. Patient living and well May 1, 1944.

CASE 3.—(Dr. Arthur Stein, New York, N. Y.) Bilateral papillary cystic tumor of ovaries in patient of 42. No evidence of peritoneal metastasis at operation (Feb. 15, 1939).

Classification. Serous papillary cystadenocarcinoma with areas of benign fibroadenoma.

Follow-up. Patient perfectly well November 30, 1942, nearly 4 years after operation. She had received postoperative x-ray treatment.

CASE 4.—(Dr. Arthur Stein, New York, N. Y.) The patient, aged 51, had been operated on in France 2 years previously with removal of both ovaries, this being preceded by two abdominal paracenteses for ascites. At second operation, January 30, 1942 (Dr. Stein), large amount of fluid evacuated, and large mass found filling pelvis, with numerous metastatic nodules of peritoneum. A piece of omentum was excised for microscopic study.

Classification. Metastatic adenocarcinoma of omentum (primary seat ovary).

Follow-up. The patient died on October 24, 1942.

CASE 5.—(Dr. John C. Henthorne, Jackson, Miss.) This patient, a colored woman, was operated upon by Dr. J. K. Avent, of Grenada, Miss., who was able to furnish only scant information. Her age was not obtainable. A vaginal hysterectomy was done (December, 1942), and the surgeon found "colloidal degeneration of the left ovary, spreading into the left broad ligament and bladder." The uterus showed multiple myomas. A second operation was contemplated later.

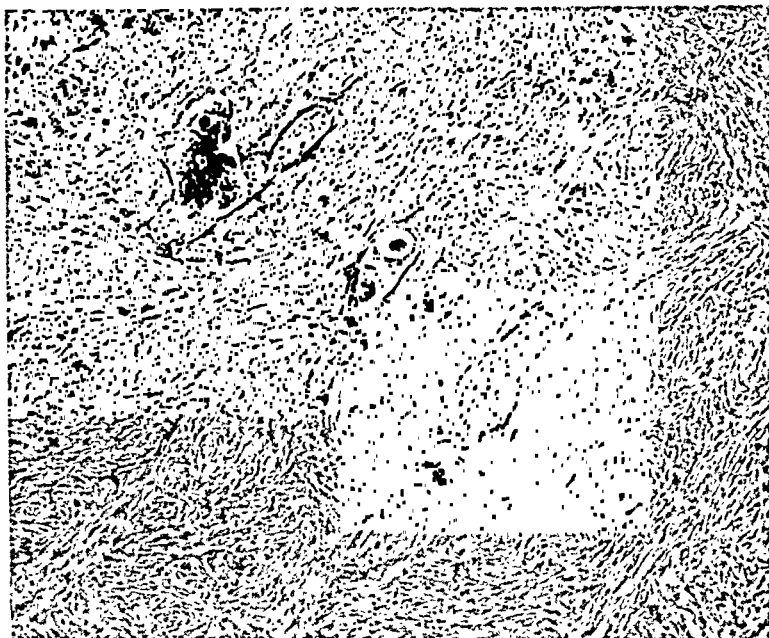


Fig. 2.—(Case 2.)

Classification. On this point, there were sharp differences of opinion among the Committee, all agreeing that the tumor was a most unusual one. Two were inclined to believe that it might be considered a mesonephroma, while one stated that "it is certainly not a mesonephroma," but that it might be a serous cystadenocarcinoma of very unusual type. The remaining two members considered it to be a tumor of mesotheliomatous type, one of these suggesting that it might be called an "endothelioma malignum."

Follow-up. Patient died 14 days after operation.

CASE 6.—(Dr. Eugene H. Countiss, New Orleans, La.) The patient, aged 11, had noticed a lower abdominal mass about December 1, 1942. No abnormal sex changes were noted. Operation disclosed a well-encapsulated, solid tumor of the left ovary, measuring 12 by 8 by 8 cm. in size. The uterus and right adnexa were normal.

Classification. Typical dysgerminoma.

Follow-up. Living and well (May 15, 1944). Now aged 13. Menstruation has not yet begun.

CASE 7.—(Dr. C. Gordon Johnson, New Orleans, La.) A tumor of ovary (received December, 1942) measuring 2.5 by 2 by 0.8 cm. associated with multiple myomas of uterus, in a patient of 43 years of age.

Classification. Typical Brenner tumor of ovary.

Follow-up. Patient living and well May 1, 1944.

CASE 8.—(Dr. Arnold Branch, St. Johns, New Brunswick.) Patient, aged 33, was operated upon December 2, 1942, on the diagnosis of pelvic inflammatory disease, retroflexion and right ovarian tumor. Right salpingo-oophorectomy and left salpingectomy were done. The right ovary was described as "like a fibroid, only slightly enlarged, retaining original shape, with no gross cysts but with some degeneration of central part."

Classification. Three of the Committee considered this a Brenner type of tumor, though all qualified this by commenting on certain unusual features, such as the adenomatous or metaplastic changes, one suggesting secondary serous cystadenomatous change. The other two members looked upon the tumor as a fibro-adenoma with metaplastic changes, one of these two considering these of rather grave import. (Fig. 3.)

Follow-up. Patient living and well as of May 15, 1944.

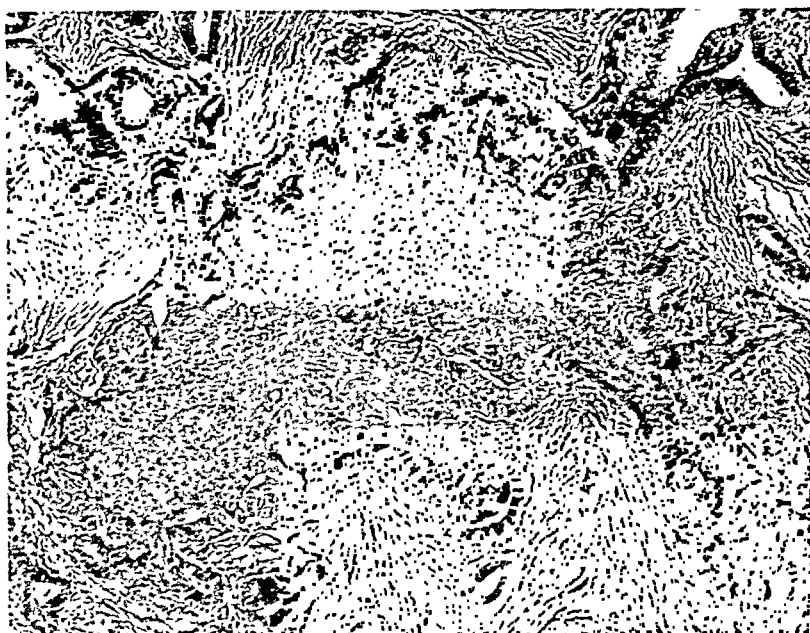


Fig. 3.—(Case 8.)

CASE 9.—(Dr. John C. Henthorne, Jackson, Miss.) Bilateral papillary tumors (operation January 18, 1943) from patient of 43, with no symptoms except some vaginal discharge for 3 months.

Classification. Histologically benign serous cystadenoma.

Follow-up. Patient living and well May 1, 1944.

CASE 10.—(Dr. Wilson Footer, San Francisco, Calif.) The material included sections from bilateral tumors of the ovaries, as well as from many other organs, obtained by autopsy from a patient of 40, the primary lesion being a gelatinous carcinoma of the sigmoid.

Classification. Krukenberg tumor of ovaries (adenocarcinoma mucocellulare).

Follow-up. This was an autopsy specimen.

CASE 11.—(Dr. John E. Hobbs, St. Louis, Mo.) Sections from a tumor of the right ovary removed by radical operation by Dr. Otto Schwarz (January, 1943) from a patient of 44, who had had irregular bleeding for 10 months, with a history of two diagnostic curettings, the first (followed by radiation) showing typical Swiss-cheese hyperplasia and the second, shortly before the laparotomy, a picture interpreted as adenocarcinoma of low grade, which opinion was shared by the majority of our Committee.

Classification. Luteinizing thecoma (Loeffler-Priesel tumor) with grade I adenocarcinoma of the endometrium.

CASE 12.—(Dr. Roy W. Hammack, Los Angeles, Calif.) A large solid tumor of right ovary weighing 920 grams from a woman of 56, in whom free bleeding had developed 3 years after the menopause. Hysterectomy with bilateral removal of adnexa on December 27, 1939. The cut surface of the tumor was described as "fasciculated, partly gray but much of it yellow."

Classification. Thecoma of right ovary.

Follow-up. Living and well December, 1940, but no later information obtainable.

CASE 13.—(Dr. Roy W. Hammack, Los Angeles, Calif.) Sections of tumor of left ovary, with diameter of about 10 cm. removed December 11, 1942, from a patient of 53, who had had hysterectomy, right salpingo-oophorectomy and left salpingectomy 14 years previously, with no bleeding since then. Section from previous operation not available.

Classification. Luteinizing granulosa cell carcinoma.

Follow-up. Developed right inguinal mass October 19, 1943, and this diagnosed as lymphoblastoma. Recession following radiation and patient fairly well in March, 1944.

CASE 14.—(Dr. Roy W. Hammack, Los Angeles, Calif.) A large partly cystic left ovarian tumor measuring 18 by 13 by 10 cm. and showing extensive necrosis, from a woman of 37. Uterus and right adnexa normal, and no peritoneal metastases at operation August 20, 1942 (left salpingo-oophorectomy).

Classification. Serous cystadenocarcinoma.

Follow-up. No definite evidence of recurrence, but much general weakness (May 15, 1944).

CASE 15.—(Dr. Karl John Karnaky, Houston, Tex.) Sections of ovary and uterus from a woman of 50. Aside from the history of bleeding, Dr. Karnaky reported as of special interest that this patient had been given 5 mg. of stilbestrol daily for 52 days. At operation February, 1942, there was a large tumor of the right ovary, the uterus was somewhat enlarged, and the left adnexa were normal.

Classification. Secondary adenocarcinoma of ovary, primary seat adenocarcinoma of uterus.

CASE 16.—(Dr. Karl John Karnaky, Houston, Tex.) A solid nodular tumor of ovary measuring 6 by 6 by 3 cm. in a woman of 40, with no menstrual or sex abnormalities—operation January 11, 1943.

Classification. Brenner tumor.

CASE 17.—(Dr. John A. Watkins, Asheville, N. C.) Bilateral "chocolate" cysts of ovaries, one said to be size of orange, the other as large as grapefruit. No clinical data. Operation January, 1943.

Classification. Endometrial cyst of ovaries (bilateral).

Follow-up. Patient living and well except for menopausal symptoms (May 15, 1944).

CASE 18.—(Dr. Robert P. Morehead, Winston-Salem, N. C.) Sections of tumor of ovary from a patient of 58, whose only symptoms were backache and vaginal discharge for 4 months, with no mention of any sex changes, though clinical data incomplete. The small ovarian tumor (received February 27, 1943) makes up three-quarters of an ovary measuring 4 by 3 by 2 cm. It is well encapsulated and of yellowish-gray color.

Classification. Luteinized granulosa cell tumor. (Two members thought the tumor to be of adrenal type.)

CASE 19.—(Dr. J. L. Goforth, Dallas, Tex.) Sections of right ovarian tumor (received March 30, 1943) from a woman of 53, who had had irregular bleeding for 6 months, the menopause having occurred some years previously. The tumor was small and spherical, yellowish, occupying the central part of the ovary which measured 4 cm. in diameter. The uterus and left adnexa were normal.

Classification. Thecoma of ovary.

CASE 20.—(Dr. C. Gordon Johnson, New Orleans, La.) The patient was a colored girl of 24, who had ceased to menstruate 8 years previously, and who developed flattening of the breasts, deepening of the voice, hirsutism, and enlargement of the clitoris. There was a tumor of the right ovary which at operation (April, 1943) measured 13 cm. in diameter. It was well encapsulated, and on section showed soft nodular areas of yellow hue, with also areas of hemorrhage. The left ovary showed a small dermoid cyst, and the uterus was normal. Supravaginal hysterectomy with bilateral salpingo-oophorectomy was done.

Classification. Arrhenoblastoma of ovary. (Fig. 4.)

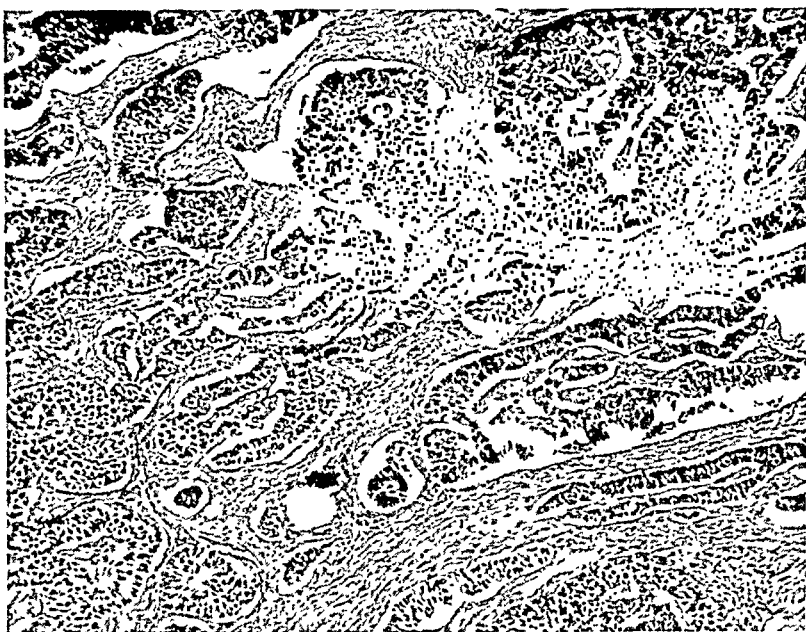


Fig. 4.—(Case 20.)

Follow-up. November 30, 1943. No indication of metastasis. Increase in weight of 22 pounds, marked increase in size of breasts; loss of much hair on abdomen, back, arms and legs, but beard still present, requiring shaving twice a week; no change in weight; some decrease in size of clitoris; vasomotor flushes 3 to 6 times daily and some night sweats. A later report (May 15, 1944) indicates that patient is living and well with no recurrence.

CASE 21.—(Dr. Robert Tennant, Hartford, Conn.) Tumor of left ovary from a woman of 65, married but never pregnant. For 1 year there had been progressive enlargement of the abdomen. The patient had always had a rather heavy beard and large clitoris, but the voice was not deep. At operation (May, 1943), 2 gallons of brownish fluid were evacuated. The tumor was partly cystic and partly solid. Supravaginal hysterectomy and bilateral salpingo-oophorectomy were done.

Classification. Mesonephroma of left ovary. (Fig. 5.)

Follow-up. Died February 23, 1944, with pelvic recurrence. No autopsy.

CASE 22.—(Dr. S. B. Pessin, Madison, Wis.) The patient was a white female of 45, with a history of enlargement of the abdomen for 6 weeks, weakness and in-

digestion. No menstrual abnormality and no sex changes. Operation (November 25, 1942) revealed a left ovarian tumor weighing about 5 pounds and measuring 22 by 19 by 11 centimeters. On section, the tumor was lobulated and showed several small cystic cavities, $1\frac{1}{2}$ to 4 cm. in diameter. X-ray showed probable metastases in the lungs.



Fig. 5.—(Case 21.)

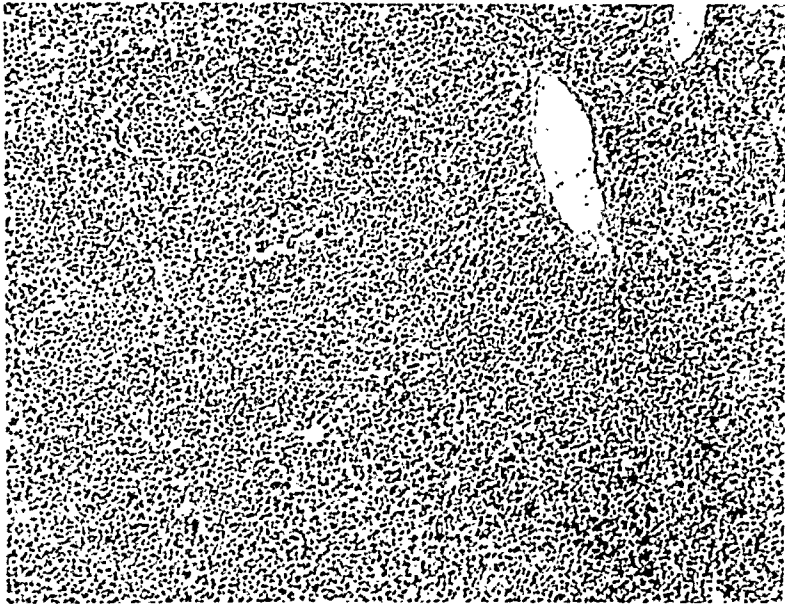


Fig. 6.—(Case 22.)

Classification. One member diagnosed lymphosarcoma, one atypical dysgerminoma, one probable dysgerminoma, one highly undifferentiated sarcoma-like arrhenoblastoma, and one was undecided between lymphoid hyperplasia, round-cell sarcoma and dysgerminoma. (Fig. 6.)

Follow-up. This patient died in November, 1943, one year after operation.

CASE 23.—(Dr. Roy W. Hammack, Los Angeles, Calif.) A large left ovarian tumor 15 cm. in diameter from a patient of 43 by Dr. J. N. Nichols on April 21, 1943. The symptoms had been abdominal enlargement, pain and some menstrual irregularity and excess. The mass was partly intraligamentous and could not be removed intact. There were some small omental nodules, up to 4 cm. in diameter. The right ovary contained a small cyst and the uterus was normal.

Classification. Adenocarcinoma of ovary.

Follow-up. Dr. Hammack reports that reoperation on November 23, 1943, showed extensive peritoneal metastasis, though patient was still living May 15, 1944.

CASE 24.—(Dr. Lester J. Bossert, Cincinnati, Ohio.) Sections of a tumor measuring 12 by 6 by 6 cm. from a colored woman of 54, whose history was that of irregular bleeding for about 6 months, beginning 8 years after the menopause. Radical operation April, 1943.

Classification. Granulosa cell carcinoma.



Fig. 7.—(Case 27.)

CASE 25.—(Dr. John C. Henthorne, Vicksburg, Miss.) Sections from an ovarian tumor (received June 24, 1943), removed by Dr. E. E. Robinson, Meridian, Miss., from a woman of 27. No other clinical data available.

Classification. Serous papillary cystadenocarcinoma.

Follow-up. Dr. Robinson reports that patient had deep x-ray therapy after operation, and was living and apparently well as of May 1, 1944.

CASE 26.—(Dr. Hans Benedict, Westwood, Calif.) Slides of hemorrhagic cyst of ovary removed (June, 1943) in very early pregnancy, the preoperative diagnosis being either ectopic pregnancy, or small ovarian cyst with twisted pedicle. Menstruation was three weeks overdue, with an acute onset of pain and tenderness.

Classification. Corpus luteum of pregnancy, old corpus luteum cyst.

Follow-up. Living and well (May 15, 1944). Pregnancy not interrupted by operation, with normal full-term delivery.

CASE 27.—(Dr. Lewis C. Scheffey, Philadelphia, Pa.) Slides from a patient of 49, who had had partial gastrectomy 7 years previously for gastric carcinoma, and who had apparently been well until recently; when she developed ascites. At the operation (July, 1943) a large solid tumor of the right ovary was revealed, its pedicle

having undergone partial torsion. The left ovary showed no tumor. There were several small uterine myomas. A complete hysteromyomectomy was done, with bilateral salpingo-oophorectomy.

Classification. Krukenberg tumor of right ovary (adenocarcinoma mucocellulare) secondary to gastric carcinoma. (Fig. 7.)

CASE 28.—(Dr. David M. Grayzel, Brooklyn, N. Y.) Slides from a tumor of the right ovary in a girl of 16 with a history of abdominal pain and gastrointestinal symptoms for about 2 months, and in whom diagnostic study led to the diagnosis of cecal tumor with cecal-colic intussusception. Operation (September, 1942) revealed a sessile tumor at the ileocecal junction, but also a tumor of the right ovary which measured 7 by 6 by 3.2 centimeters. The structure and microscopic appearance of the intestinal and ovarian tumors were identical.

Classification. Lymphosarcoma of right ovary, secondary to intestinal lymphosarcoma. (Fig. 8.)

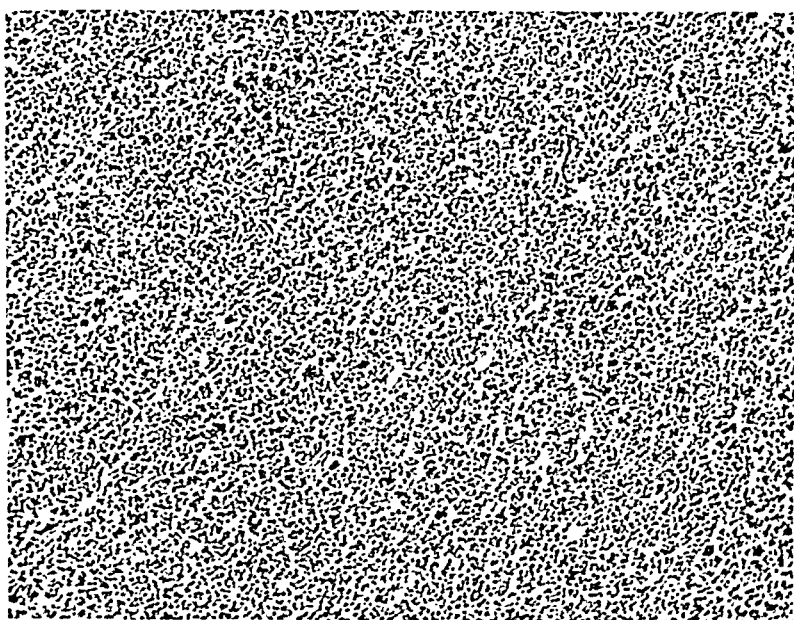


Fig. 8.—(Case 28.)

Note: Dr. Grayzel later reported that a similar tumor recurred in the left ovary, and was removed with panhysterectomy in July, 1943, ten months after the first operation. The patient was apparently well in September, 1943 (subsequent follow-up note to be obtained).

Follow-up. Patient perfectly well on May 1, 1944.

CASE 29.—(Dr. Lester J. Bossert, Cincinnati, Ohio.) An ovarian tumor (received September, 1943), 20 cm. in diameter from a patient of 22, whose history was said to be entirely negative except for the presence of some lower abdominal enlargement, noted a few weeks previously. The pelvic organs were normal except for the unilateral tumor.

Classification. Dysgerminoma of ovary.

CASE 30.—(Dr. Lawrence Chaffin, Los Angeles, Calif.) An ovarian tumor 7 cm. in diameter, with a light-yellowish friable cut surface, in a patient of 50 who entered the hospital in shock, with severe abdominal pain beginning 5 hours previously. The previous history was negative except that menstruation for the past 10 years had been somewhat more profuse than formerly. Operation on August 15,

1943, disclosed the right ovarian tumor, the left ovary being normal. The abdomen contained 3,000 c.c. of liquid blood and 1,000 c.c. of clots, the source being a 5 cm. gaping tear on the surface of the tumor. There was no history of trauma or unusual exertion, save possibly straining at stool a short time before the onset.

Classification. Granulosa cell tumor of right ovary. (Fig. 9.)

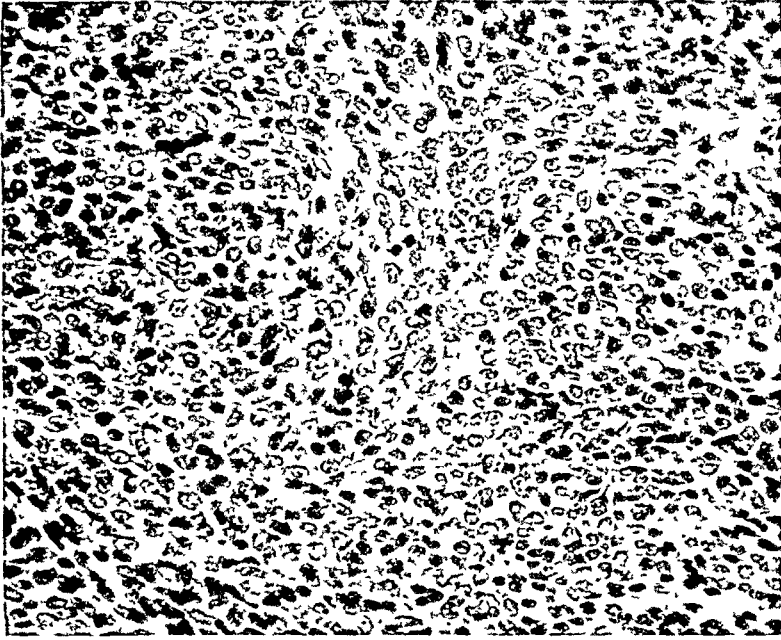


Fig. 9.—(Case 30.)

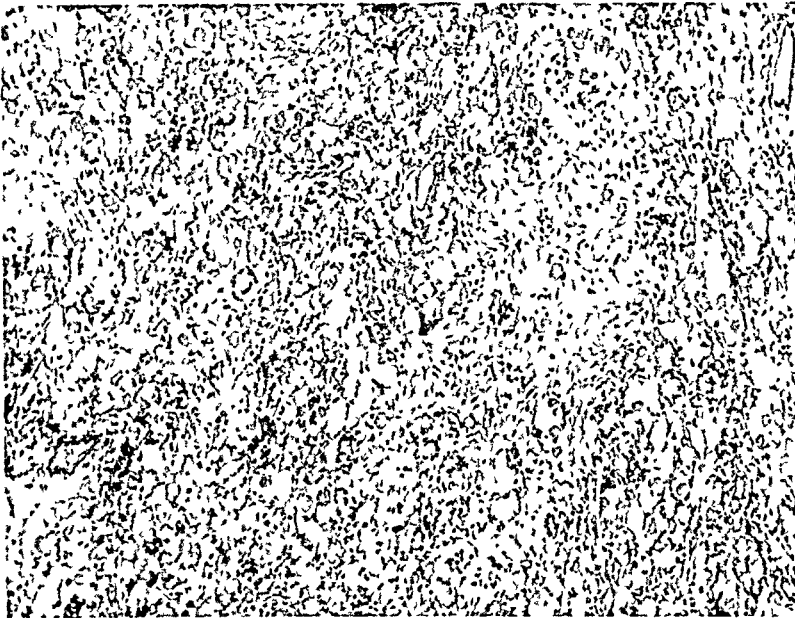


Fig. 10.—(Case 31.)

CASE 31.—(Dr. J. M. Moore, San Antonio, Tex.) A tumor of the left ovary, measuring 6 by 5 by 5 cm. removed from a patient of 36, who had been having severe pain in the left humerus for 1 year, although x-ray study showed no bone pathology, according to her physician, Dr. K. B. Round, of San Angelo, Texas. The gastrointestinal history was said to have been entirely negative. Menstruation had

always been normal except for menorrhagia with the last period, August 3, 1943. Dr. Moore reports that at operation, on August 15, 1943, a left ovarian tumor was found.

Classification. Krukenberg tumor of left ovary. (Fig. 10.)

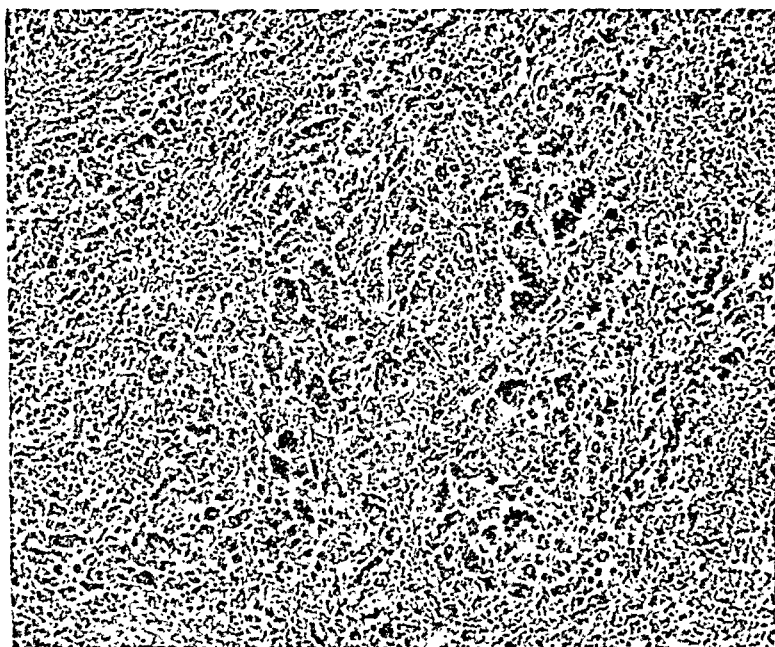


Fig. 11.—(Case 32.)

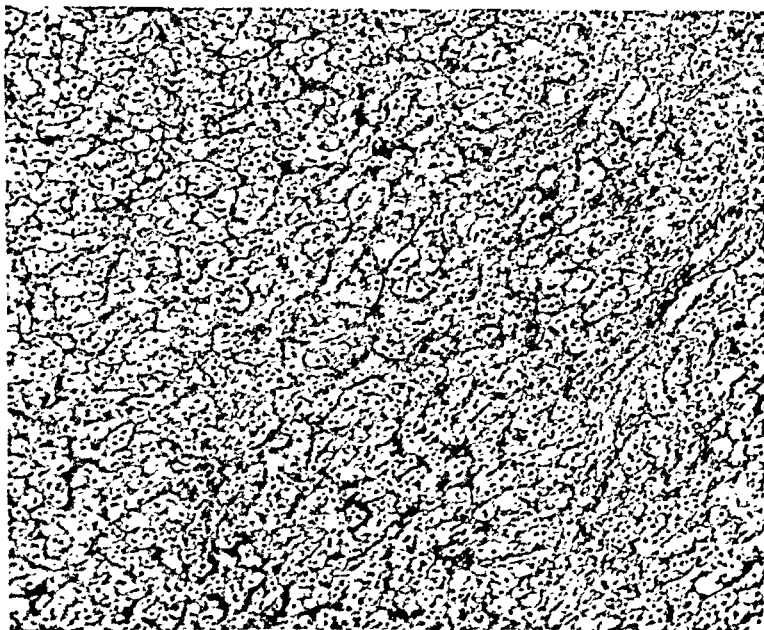


Fig. 12.—(Case 33.)

CASE 32.—(Dr. William E. Ehrlich, Philadelphia, Pa.) Slides from a right ovarian tumor 12 by 10 by 5.5 cm., removed from a colored patient of 49, whose complaint was of menstrual irregularity (intervals 2 to 6 weeks) and menorrhagia with some periods, though others were scanty. A firm pelvic mass reaching to the umbilicus was thought to be a fibroid uterus, but operation September 26, 1943, revealed a solid ovarian tumor. A right salpingo-oophorectomy was done.

Classification. Granulosa cell carcinoma of right ovary. (Fig. 11.)

Follow-up. No information since October 8, 1943, when patient was in good condition.

CASE 33.—(Dr. Philip Rosenblatt, Brooklyn, N. Y.) A tumor of the right ovary from a 31-year-old prostitute with gonorrhea and syphilis. She had had amenorrhea for 10 years, with the development of typical masculinizing symptoms, including marked hirsutism (daily shaving), deep voice, and enlarged clitoris. Urinary studies revealed 23.1 mg. androgen excreted in 24 hours, with no prolactin or estrone. A tumor mass was palpable in the left ovarian region. At operation (November, 1943) this proved to be a dermoid cyst 5 cm. in diameter, and this was removed.

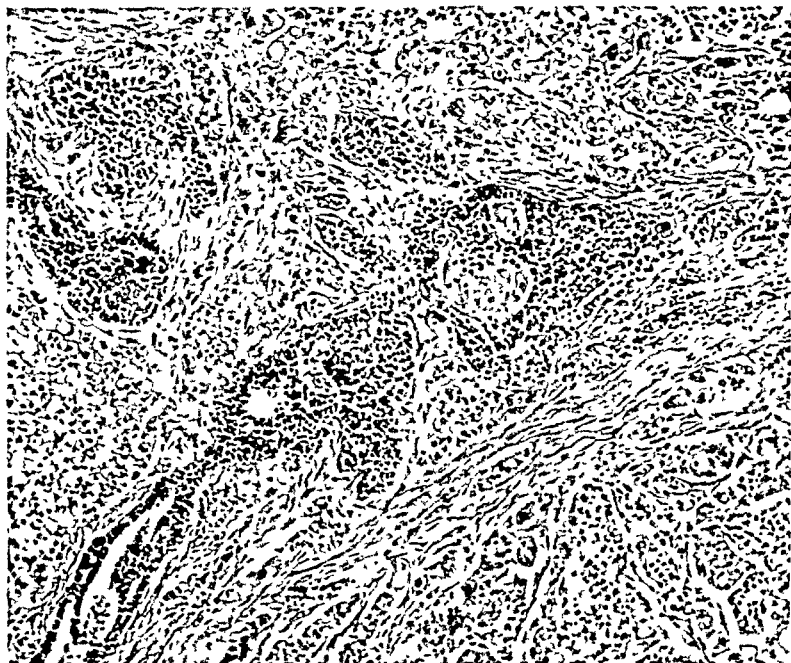


Fig. 13.—(Case 34.)

The right ovary, however, was found to be the seat of a soft mass 8 cm. in diameter, and this was removed with most of the ovary. On hemisection, the surface was soft and bulging, and of bright-orange hue, surrounding a central depressed area of firmer gray tissue. Later study revealed a small dermoid cyst in this ovary also, in addition to the above described mass.

Classification. Adrenal tumor of right ovary, with bilateral dermoid cysts (coincidental). (Fig. 12.)

Follow-up. Patient living and well. Androgen negative; estrogen 4.8 mg. (March 3, 1944).

CASE 34.—(Drs. James M. Wilson and C. C. Douglass, Durham, N. C.) Sections, with very complete clinical history, autopsy protocol and photographs from a widely metastasizing tumor, presumably of ovarian origin, in a colored patient of 49, the original diagnosis being dysgerminoma. The chief points in the history were a skipping of alternate menstrual periods, for 6 months before admission, and the appearance of a lower abdominal mass 3 months before she entered the hospital. Later, there was considerable pain and a loss of weight of something like 30 pounds. After thorough study, an exploratory laparotomy was done, revealing a large adherent mass in the region of the left ovary, the uterus being enlarged and studded with tumor masses, as was the undersurface of the diaphragm. It was possible to

remove the left adnexa but not the uterus or the right-sided mass, because of their extreme fixation. The patient died on the third postoperative day. The autopsy showed the left-sided mass, as above described, apparently replacing the left ovary. There were about 1,000 c.c. of fluid in the abdominal cavity. Metastases were present on the intestines, in the left kidney and adrenal, the uterus and at various other points. The microscopic appearance of the tumor is shown in Fig. 13.

Classification. Here again, it is necessary to record wide variations in opinion. Two members agreed with the original diagnosis of dysgerminoma, although one of these expressed doubt of this because of the papillary structure seen in the pulmonary metastases. Another states, "It is certainly not a dysgerminoma," his own impression being that the tumor is a medullary carcinoma, of unknown origin. A fourth considers the growth is "neither a primary ovarian nor uterine tumor," but that it is of primary peritoneal origin—"mesothelioma peritonei malignum." The fifth diagnosed metastatic ovarian carcinoma from an indeterminate primary situs.

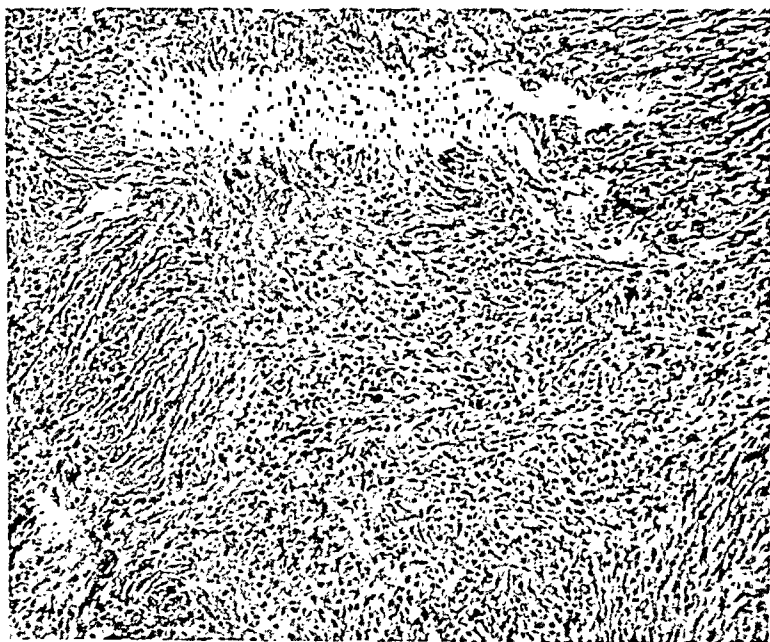


Fig. 14.—(Case 36.)

CASE 35.—(Dr. David B. Cheek, Baltimore, Md.) This patient, a 49-year-old colored woman, had had a normal menopause 3 years previously. A four-day period of menstruation-like bleeding recurred 3 months before admission and again 4 days before she entered the hospital. A left-sided mass, irregular, nodular and adherent, was made out on pelvic examination. Operation on October 26, 1943, showed the pelvis filled with a friable, lobulated mass apparently arising from the lateral pole of the left ovary. It was not possible to remove the tumor mass completely, because of its invasion into the tissues of the lateral pelvic wall and elsewhere.

Classification. Granulosa cell carcinoma.

Follow-up. Has received deep x-ray therapy, but general condition poor on May 1, 1944.

CASE 36.—(Dr. Lawrence Parsons, Reno, Nev.) Sections from a small ovarian tumor (received September, 1943), 2.5 cm. in diameter from a patient of 34 whose only symptom was irregular bleeding. The flow was described as persisting for 5 to 7 days, with cessation for only a few days, and again recurrence of bleeding, this sequence having been present for the past year.

Classification. Thecoma (Loeffler-Priessel tumor). (Fig. 14.)

Follow-up. Living and well, with no recurrence (May 15, 1944).

CASE 37.—(Dr. Edward L. Krieg, Baltimore, Md.) Slides from the ovary of a patient of 37, an unmarried Catholic Sister, who had had hysterectomy and unilateral salpingo-oophorectomy October 1, 1943, because of profuse functional bleeding. As there was also considerable abdominal discomfort, x-ray study of gastrointestinal tract and other studies had been made, all with negative findings, a diagnosis of

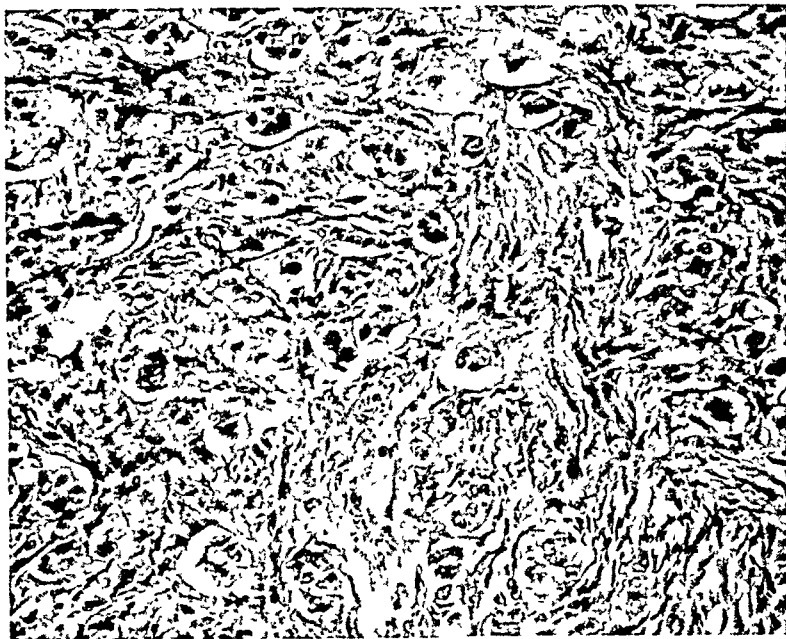


Fig. 15.—(Case 37.)



Fig. 16.—(Case 38.)

probable chronic recurrent appendicitis being made and appendectomy included in the operation. Palpation of abdominal organs at operation showed no evidence of any neoplasm. The ovary was grossly normal, the lesion under study being of microscopic nature. Its appearance is shown in Fig. 15.

Classification. One member made a diagnosis of granulosa cell tumor as did a second who affixed a question mark to this diagnosis, and later sent in a revised

diagnosis of metastatic adenocarcinoma from some other site, possibly the stomach. Three other members were inclined to the impression of metastatic adenocarcinoma, although one of these wondered if it could not be an arrhenoblastoma.

Follow-up. Patient died of pneumonia 1 week after operation. No autopsy.

CASE 38.—(Dr. John E. Hobbs, St. Louis, Mo.) Slides (received September 20, 1943) from a patient of 78, who for 4 months had had increasing weakness and pallor, with swelling of the lower abdomen. There had been no bleeding since the menopause at the age of 52. At operation (Dr. F. P. McNalley), a large semi-necrotic and semicystic tumor of the right ovary. It was very friable, tearing in removal, permitting the escape of about 500 c.c. of dark bloody fluid. There were numerous small metastases studding the pelvic peritoneum. The microscopic appearance is shown in Fig. 16.

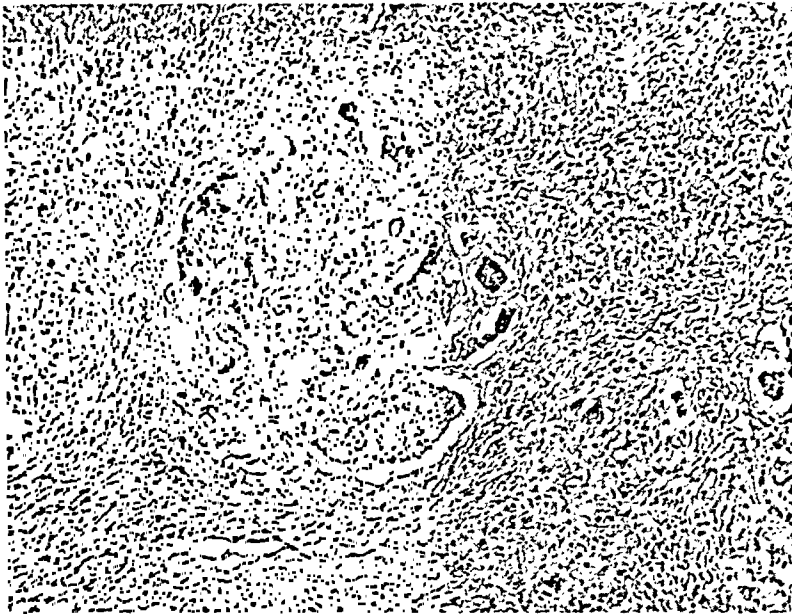


Fig. 17.—(Case 41.)

Classification. One member diagnosed malignant thecoma, one sarcoma, one fibroma and one considered it "unquestionably a malignant dysgerminoma." The fifth member first called the tumor neurinoma, but after further study, changed this to glioma of teratomatous origin.

Follow-up. Dr. McNalley reports that examination April 29, 1944, showed patient living and well, with no sign of recurrence and gain of 5 pounds in weight.

CASE 39.—(Dr. W. D. Stovall, Madison, Wis.) A large cystic ovarian tumor removed from a woman of 46. No clinical data. Slides received December 16, 1943.

Classification. Cystic fibroma of ovary.

CASE 40.—(Dr. W. D. Stovall, Madison, Wis.) A tumor about the size of a lemon in a 26-year-old woman. The ovary was apparently not itself involved, as the tumor was attached to it by a pedicle. The growth had a yellow color, "as if there were fat around it, but the cut surface did not have usual yellowish appearance of thecomas." Slide received December 16, 1943.

Classification. Fibroma of ovary with edema and necrosis.

CASE 41.—(Dr. W. D. Stovall, Madison, Wis.) An ovarian tumor weighing 2,000 Gm., essentially solid, but containing some cystic spaces. Slides received

December 16, 1943. The patient was 19, and suffered with dyschondroplasia and hemangiomatosis (Maffucci's syndrome). She had fairly well-developed secondary sex characters, but had been amenorrheic for 9 months before laparotomy.

Classification. Three members diagnosed mesonephroma of the ovary, one granulosa cell carcinoma and one teratoma. (Fig. 17.)

Follow-up. Patient living and apparently well May 1, 1944.

CASE 42.—(Dr. David R. Meranze, Philadelphia, Pa.) A tumor of the left ovary (received December 15, 1943) from a woman of 42, unmarried, with a history of pain in the left lower abdomen, no menstrual disorder, no feminizing or masculinizing changes. The tumor was a multilocular cyst 11 by 10 cm. to which was intimately attached a large strikingly orange-yellow solid tumor 7 by 5 by 3 cm. in size.

Classification. Pseudomucinous cystadenoma with fibroma.

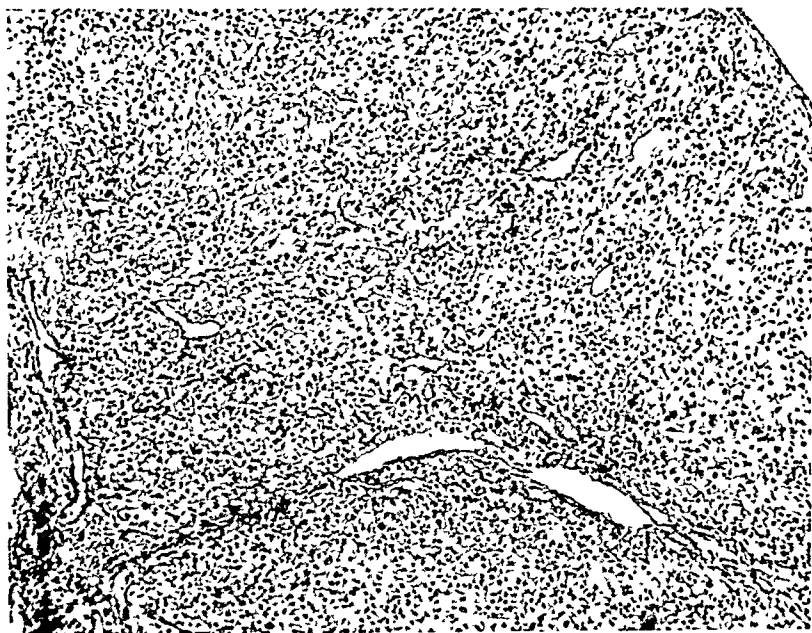


Fig. 18.—(Case 44.)

CASE 43.—(Dr. John C. Henthorne, Vicksburg, Miss.) Biopsy sections obtained January 6, 1944, from an ovarian cystic tumor with warty nodules in its wall. The patient was a colored woman of 43, no other data being available.

Classification. Serous papillary cystadenocarcinoma.

CASE 44.—(Dr. Joseph A. Burket, Louisville, Ky.) Sections and tissue from a tumor (received December 18, 1943) in a 36-year-old woman who had noted enlargement in her abdomen and who had lost 40 pounds in weight during the preceding year, presumably through dieting. She had not menstruated since the birth of her second child 16 years before. Shortly after this childbirth, she had developed heavy hirsutism, requiring daily shaving. The abdomen was filled with a multinodular tumor, arising from the left ovary. The preoperative diagnosis was arrhenoblastoma. The uterus was four times the normal size, the right ovary was normal, and the liver was much enlarged, containing many large and small nodules. The spleen was five times the normal size. The ovarian tumor measured 16 by 13 by 8 cm., and on section showed numerous rounded or irregular areas of various colors, some reddish-gray, some yellow and others hemorrhagic. There was considerable stroma. Following operation the patient declined, with the development of jaundice

and death on the eleventh postoperative day. Vaginal bleeding appeared on the ninth day, the first time in 16 years. Autopsy was not obtainable.

Classification. Adrenal tumor of ovary (hypernephroma). (Fig. 18.)

Follow-up. Patient died on eleventh postoperative day.

CASE 45.—(Dr. Clement R. Munroe, Pinelhurst, N. C.) Sections from a large ovarian tumor removed in 1935 from a colored child of 6, who presented the picture of precocious puberty. After removal of the tumor, the abnormal symptoms disappeared completely.

Classification. Granulosa cell tumor of ovary. (Fig. 19.)

Follow-up. Dr. Monroe reports that a recent examination (8 years after operation) showed the girl to be entirely normal with no sign of recurrence. Menarche had occurred at 12, and there has been no abnormality of menstruation.

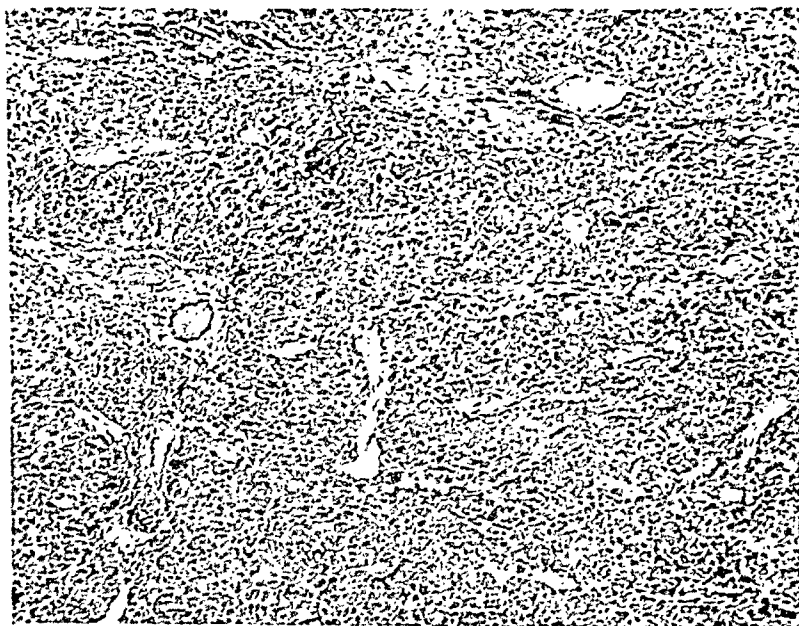


Fig. 19.—(Case 45.)

CASE 46.—(Dr. R. W. TeLinde, Baltimore, Md.) The patient, aged 27, had been operated upon in 1929 at age of 12 for a Ewing's tumor of the cranial bones, with localized recurrence in 1930, followed by secondary operation and x-ray therapy at intervals until 1935, with no evidence of further recurrence until 1942, when she developed metastases in the lungs. These have responded readily to irradiation, but have never completely disappeared. Menstruation normal until October, 1943, when she developed midinterval bleeding lasting 3 to 7 days. Examination revealed a large mass pushing the uterus anteriorly and feeling like a benign fibroid. Operation revealed a solid tumor arising from the left ovary and filling the pelvis. There were two implants at the bladder reflection of the peritoneum. No other metastases were found. Supravaginal hysterectomy with double salpingo-oophorectomy were done.

Classification. One member diagnosed metastatic Ewing's tumor, one thought the picture consistent with such a diagnosis but hesitated in giving an opinion without sections of the original tumor, one declined to offer a diagnosis because he thought the tumor too retrogressive, and one hesitantly thought it a granulosa cell tumor, and the fifth member likewise called it a granulosa cell carcinoma. (Fig. 20.)

Follow-up. General condition May 1, 1944, reported as poor by her physician in North Carolina. She has recently had several transfusions because of marked anemia.

CASE 47.—(Dr. Robert Tennant, Hartford, Conn.) An unmarried woman of 37 had noted a lump in the abdomen. No menstrual disorder except that last period had occurred one week before expected date. At operation on October 6, 1943, the tumor replaced the left ovary. It was solid, measuring 12 cm. in diameter, with irregular lobulation, and a yellowish cut surface. The remaining pelvic organs were normal. Panhysterectomy and bilateral salpingo-oophorectomy were done.

Classification. Dysgerminoma of ovary.

CASE 48.—(Dr. A. L. Pietrolongo, Philadelphia, Pa.) Tumor 5 cm. in diameter replacing one ovary (received July 13, 1943). It was stony hard, lobulated, well encapsulated, with a dense yellowish-brown and trabeculated cut surface. The tumor was found at operation for multiple fibroids of the uterus, the patient being 47 years old.

Classification. Brenner tumor.



Fig. 20.—(Case 46.)

CASE 49.—(Dr. Lawrence Wharton, Baltimore, Md.) A large tumor of the left ovary, involving the sigmoid, removed from a woman of 58, on February 19, 1944. Radical removal of the pelvic organs, with resection of 15 cm. of sigmoid. The right ovary was normal, but omental metastases were present.

Classification. Granulosa cell carcinoma of ovary.

Follow-up. Patient still in good condition June 1, 1944 (only 3½ months after operation).

CASE 50.—(Dr. Caspar G. Burn, Brooklyn, N. Y.) The patient, aged 53, was admitted first on May 10, 1943, again on July 21, and once more on September 28. There was a lower abdominal mass which had increased since her first examination. Operation on December 13, 1943, revealed a large adherent ovarian cyst containing 2 liters of bloody fluid. Supracervical hysterectomy, right salpingo-oophorectomy and left salpingectomy were done. Postoperatively the patient went into shock and died on January 8, 1944.

Classification. Granulosa cell carcinoma of ovary.

Follow-up. Patient died on twenty-sixth postoperative day.

Comment

While the work of the Committee on Ovarian Tumors is as yet in its very infancy, it is already evident that its possibilities are great, and that it is worthy of the cooperation of all gynecologists and pathologists. Plans are under way to publicize the project more widely through direct appeal to many who should be in a position to supply much of the kind of material which is being sought. It should be emphasized that it is not only the rare tumors or those presenting difficulties in diagnosis which are appealed for. To illustrate, the very common serous papillary cysts are of special interest because of the frequent uncertainty of prognosis, not to speak of the considerable group of these cases in which pathologists will differ as to the diagnosis of histologic malignancy or nonmalignancy.

The best possible clinical data and the best possible material for study, in the form of slides, blocks of tissue or entire specimens, are desirable, as has been emphasized in the various announcements issued by the Committee. Finally, to quote from the last of these, "The Registry is to be looked upon as a cooperative project among the gynecologists and pathologists of the country, and it is earnestly hoped that all will develop the routine of sending material from all interesting ovarian tumors, with adequate clinical data to the Committee for study and registry."

26 EAST PRESTON STREET

Discussion

DR. JOE V. MEIGS, BOSTON, MASS.—To me this first glimpse of the Ovarian Tumor Registry has been very enlightening. The number of doctors participating and their geographical distribution shows with what importance the whole country looks upon such an endeavor. No doubt, after the publication of the Committee's report, a great many more cases will come to the Registry for consideration.

The value of having histories, pieces of tissue and follow-up is borne out by the cases presented today. For years, I have doubted the frequency of granulosa cell tumors of the ovary but in this group of 50 cases granulosa cell tumors comprise 18 per cent, and with thecomas added, 26 per cent. This is fairly good proof that these tumors are much more frequent than I have ever suspected. It had been my opinion that they represented but 5 per cent of the ovarian tumors, exclusive of the simple cysts.

I have also been impressed by the apparent lack of radical surgery in these cases. It is my opinion, that in a suspected case of cancer of the ovary, bilateral oophorectomy and total hysterectomy ought to be carried out if at all possible. Cancer of the ovary is, or will be, bilateral in at least 40 per cent of cases and therefore bilateral oophorectomy is essential. In the definitely endocrine type of tumor, radical surgery is not necessary for in these metastases are few, if the tumor has not already become adherent. Endocrine tumors are not frequently bilateral.

I am delighted with the report and feel that the Registry should be encouraged to continue its fine work. Important clues as to the histogenesis, proper treatment and prognosis must be forthcoming from such a wonderful group of tumor cases.

DR. JOHN L. McKELVEY, MINNEAPOLIS, MINN.—This is a difficult paper to discuss if one is to speak of the material that has been presented. It is probably correct to say that most of the members of this Society have been curious to know of the progress of the Ovarian Tumor Registry, and that they have sincerely hoped that it might take its place as a source of useful information. There is reason

to believe that this hope will be justified. Dr. Novak has drawn attention to the experiences of the initial period of the Registry's activity. These have produced some surprises and some useful lessons have been learned.

It would seem clear that a well-organized Ovarian Tumor Registry is worthy of the sponsorship given by this Society and of the considerable efforts put forth by the members of the Committee responsible for it. As such, it merits the participation of the members of the Society as a whole. Perhaps the Society is awaiting the example of the members of the Committee themselves.

The aims of the Ovarian Tumor Registry are clear. Too much time must elapse before the material of any single clinic may be expected to produce an adequate sample of the rare and more interesting tumors. To have these available in large numbers for study is obviously desirable. Certain requirements should be satisfied, however, if the material is to be useful for study purposes. The clinical requirements can probably be readily met. A careful and complete clinical history, accurate description of the findings at surgery and prolonged follow-up or autopsy report are not difficult to obtain.

Dr. Robert Meyer who is one of the members of your Committee has asked me to bring to your attention some features of the organization of the Registry which bear particularly upon the histological problems.

The material which has been coming through is made up largely of already stained and mounted sections. A very large part of this is astonishingly poorly prepared. Diagnosis is difficult enough, and much of it is useless for study. It does not appear to be widely recognized that many ovarian tumors show extensive variations in different areas, and that patient search of the tumor may be essential to a proved decision. Careful and often multiple differential staining may not infrequently be necessary. Any future study will certainly require that adequate amounts of fixed tissues be available. Altogether, it would seem wise to suggest that the policy of collecting only already prepared sections be changed. Better results could be obtained if a collecting laboratory were to request reasonable samples of the original material, and to prepare it adequately. The direct availability of unstained sections would greatly aid the members of the Committee in arriving at an objective conclusion. This is no field for guessing, and poorly prepared material may present hazards which can lead to little else.

This is not the place to argue about the details of differences of opinion in the interpretation of the material presented. It might, however, be suggested that the Committee could perform a useful function if it could find a basis for agreement upon certain moot points in the ovarian tumor field. The vexing problem of the confusion which exists as between the fibroma and the theca-cell tumor does not appear to be insoluble. The term Krukenberg tumor is used in this report in a sense which will bear examination. At least, some sort of agreement or understanding is desirable. And finally, if for no other reason than for the sake of the worried student, it would be well to agree upon the spelling of dysgerminoma.

Dr. Novak and his Committee have conscientiously carried out the organization of what promises to be a productive and interesting enterprise. I should like to express an appreciation of their efforts and an interest in their work.

The second installment of the American Gynecological Society Transactions will appear in the January, 1945, issue of the JOURNAL.

Department of Reviews and Abstracts

Selected Abstracts

Radiation

Thomas, Sydney: Diffuse Calcification of the Placenta Demonstrable in Vivo, Radiology 41: 573, 1943.

The author describes a case of diffuse calcification of the placenta demonstrable by x-ray and the use of a new technique. It is felt that with this method other special procedures such as iodide or air cystography may be eliminated in the roentgenologic diagnosis of placenta previa.

WILLIAM BERMAN.

McIntosh, Harriet C.: Roentgen Therapy of Pelvic Tuberculosis in the Female, Radiology 42: 48, 1944.

The author considers only surgical and radiation therapy in his discussion. In regard to roentgen therapy, treatment should not be given merely because of a presumptive diagnosis of tuberculosis. An adequate diagnosis should be made either by curettage or by laparotomy. The use of surgery and its limitations are mentioned. Limitations in regard to x-ray therapy are also stated. X-ray has no effect on pyosalpinx, ascitic fluid or abscess material. It is of value in the dry form of peritonitis, or after the fluid has been removed postoperatively. Protection of the ovaries should be considered in the technique of treatment during the child-bearing period. In advanced tubal-peritoneal disease, the combined radiologic and surgical treatment is indicated. The worst prognosis is in cases with severe disease elsewhere. Different techniques of various authors are mentioned. The author reports 11 cases with 6 patients clinically free of disease 1 to 3 years, and 4 more showing local improvement.

WILLIAM BERMAN.

Maxfield, Jr., J. R., McIlwain, A. J., and Robertson, J. E.: Treatment of Radiation Sickness With Vitamin B₆ (Pyridoxine Hydrochloride), Radiology 41: 383, 1943.

After perusal of the literature in regard to vitamin therapy for radiation sickness, the authors tried pyridoxine hydrochloride intravenously. They began by giving 25 mg. intravenously every day, only in cases in which radiation sickness was definitely present. In many cases, only one dose was necessary to stop the unfavorable symptoms. The authors now recommend that after the onset of radiation sickness 25 mg. be given intravenously immediately, and repeated at intervals of twenty-four to seventy-two hours as needed throughout the remainder of the treatment series. This particular treatment does not preclude the use of such other medications as may be needed. The use of liver extract, a high vitamin intake, sedatives, etc., are to be used when indicated.

WILLIAM BERMAN.

Miscellaneous

Leftwich, William B., 1st Lt. U.S.M.C.: An Intradermal Test for the Recognition of Hypersensitivity to the Sulfonamide Drugs, *Bull. Johns Hopkins Hosp.* 74: 26, 1944.

A method has been described by which positive skin tests may be obtained in patients who have shown hypersensitive reactions to the sulfonamide drugs. The material used for the skin test consisted of serum obtained from patients who were receiving a sulfonamide therapeutically and contained a drug level of from 2 to 25 mg. per cent. This skin test is simple to perform, may be easily and quickly interpreted, and was found to be reliable in the diagnosis of drug sensitivity in 28 out of 30 cases of definite drug reactions. It is hoped that this test may be useful, both in the differential diagnosis of drug reactions, and perhaps as a precautionary measure before starting sulfonamide therapy in patients who have previously received one of these compounds. The fact that positive skin tests may be so consistently obtained in sensitive individuals is additional evidence that drug sensitivity is an allergic reaction. The sensitizing antigen may be a sulfonamide plasma protein combination which occurs in vivo in the circulating blood of patients during sulfonamide therapy, the sulfonamide perhaps acting as a haptene. The failure of two patients in the experiment who developed hepatitis, and one patient who developed hemolytic anemia as a result of sulfonamide therapy, to show positive skin reactions for the homologous sulfonamide, supports the belief that these latter reactions are due to direct toxic action of the sulfonamide rather than to hypersensitivity.

C. O. MALAND.

Brown, Willis E., Gunderson, Millard F., Schwartz, Pauline, and Wilder, Violet M.: A Clinical and Bacteriologic Study of Phemerol as a Skin Antiseptic, *Surg., Gynec. & Obst.* 78: 173, 1944.

The authors present a series of studies on the comparative value of various skin antiseptics in common use surgically. Of particular interest was one of the detergent group, namely phemerol. The technique used in the study was based on the use of small blood agar plates placed on the abdomen, and then removed at half-hourly intervals and incubated at 37° C. for 48 hours. The count of the number of colonies gave an index of the effectiveness of the antiseptic. A basic wash of green soap and alcohol was applied to the whole abdomen. One-half only was painted with the substance to be tested, the other serving as a control. When tested by this method, phemerol was found to be superior to the mercurials studied, but about equal to tincture of iodine.

L. M. HELLMAN, LT. M.C., U.S.N.R.

Lee, Roger I.: Geriatrics: The Medical Care of the Elderly, *New England J. Med.* 230: 190, 1944.

In a beautiful and humorously worded article, the author takes up the subject of geriatrics, pointing out its great importance and the fact that it is at the stage where pediatrics was a generation ago.

Advances in medicine and public health which apply almost entirely to infancy and youth, have lengthened the average expectation of life to 64 years to a person born in 1943. But the added years really represent a salvage of infants and youths, not of adults.

The author points out in his early days as a physician, old people were stored away so to speak in lace caps or bedroom slippers and not permitted any social activities. He welcomes the modern trend in the opposite direction, but deplores the

extremes. He enumerates the degenerative processes which accompany old age, the diminution of the secretions of the alimentary tract, the prevalence of gallstones and diverticulosis. He feels that diet is of great importance, aided by vitamins, and in certain selected cases thyroid extracts, iodides, and in special cases sex hormones.

JAMES P. MARR.

Anatomy, Anomalies, Etc.

Uranga, F. A., and Dubrovsky, I. R.: *Fetus Compressus*, *Semana méd.* 50: 1463-1466, 1943.

Death and retention of a twin, which is not recognized during pregnancy, are unusual and infrequent occurrences. Its retention, even to the time of parturition of the twin that develops normally, depends on the time of fetal death. If this occurs within the first three months, when the embryo contains much water and is friable, dissolution occurs. Afterward, from three to five months, mummification, and later maceration and even putrefaction occur, when microorganisms invade the uterine cavity. When the fetus becomes mummified, it is compressed between the uterine wall and the developing embryo, to form what is called fetus papyraceous or compressus.

In a series of 61,998 births, the authors found three instances of fetus compressus. In the same series there were 929 sets of twins. In all three instances, the pregnancies were dizygotic and in all, continuation of strong contractions revealed unexpectedly the presence of a mummified fetus. All showed development of an embryo at about three months. In two cases, a living normal infant was delivered. In the third, the fetus was stillborn at about eight and a half months. In no instance had there been any unusual symptoms during gestation to suggest such an occurrence.

Fetal death in these cases is usually explained on the basis of difficulty of nutrition of twins. The changes that occur have been described by Lempereur. The fetus dies in the amniotic cavity like fruit in alcohol. The tissues contract and condense, the embryo decreases in size, and is reduced to a fragile shell, and becomes hard and dry. The fetus takes on a yellowish-gray color. The amniotic fluid disappears by absorption and deposits a sediment on the fetus. Usually discovery of a fetus compressus is not made until parturition.

J. P. GREENHILL.

Quisenberry, Walter B.: *Spina Bifida and Polydactylysm in One-Egg Twins*, *Virginia Monthly* 71: 303, 1944.

Twins born to a Negro woman in her third pregnancy after two normal deliveries of normal babies is reported. The twin babies were similar in that each weighed 4 pounds, each possessed two erupted incisor teeth, and each had a spina bifida with meningocele of the same extent. They differed in that one had a well developed polydactyle (thumb). The twins were undoubtedly single ovum as evidenced by the similarity of their defects with the exception of the polydactylism, and there was a single ovum with no amnion between the babies in utero. Both died shortly after birth. Some theories as to possible etiology of spina bifida are presented.

WILLIAM BICKERS.

Trotter, Mildred and Letterman, George H.: *Variations of the Female Sacrum: Their Significance in Continuous Caudal Anesthesia*, *Surg., Gynec. & Obst.* 78: 419, 1944.

Six hundred and seventy-four sacra from white and Negro females were examined. The variations in length and diameter of the sacral canal and measurements of the

hiatus are described. Certain abnormalities of the canal and hiatus which would make the use of continuous caudal anesthesia difficult or impossible are demonstrated by photograph and anatomic description. In 45 per cent of the pelves, the upper end of the hiatus reached a level cephaled to the lower third of the body of the fourth sacral vertebra. Theoretically, this reduces the distance from the highest possible point of insertion of the needle and the inferior limit of the subarachnoid space. In 22 per cent, there were congenital deficiencies in the dorsal wall of the canal which might permit the exit of the needle, and thus a failure of the anesthesia. In 5.5 per cent, the anteroposterior diameter of the canal was less than that of the needle commonly used, making a caudal impossible.

L. M. HELLMAN.

Rodiles, A. Q.: *The Pelvis of Mexican Women*, *Obst. y. ginec. latino-am.* 1: 466-470, 1943.

From an extensive study over a period of 20 years, the author comes to the conclusion that in spite of the small size of the Indian females in Mexico, their pelves are as normal as those of white women. Contracted pelvis is rarely found and normal labor is almost invariable.

J. P. GREENHILL.

Anesthesia, Analgesia

De Araujo, J. Onofre: *Particularities of Anesthesia in Obstetrics. Consideration of 886 Anesthesias During the Five-Year Period of 1939 to 1943*, *An. brasil. de ginec.* 16: 428-437, 1943.

According to the author the use of anesthetics in obstetrics differs from that in surgery, and he emphasizes the difficulty of selecting a good anesthetic for all purposes because of the conflicting interests of mother and baby. He distinguishes between analgesia and anesthesia.

Regarding analgesia, he calls attention to the danger of administering drugs to relieve the pain because of their bad effects on the respiratory center of the newly born; morphine, especially, must never be given during the two or three hours preceding delivery. The use of so-called twilight sleep and of continuous caudal analgesia was discontinued because of the unreliable results obtained in their experimental applications. In selected cases, nitrous oxide may be permitted during the second stage of labor, provided that it is administered by an expert anesthetist and under the supervision of the obstetrician.

Regarding anesthesia, the author advocates the use of spinal anesthesia in cesarean section because it favors uterine retraction; however, owing to the risk of death of this anesthesia which seems to be unavoidable and caused by the introduction of the drug into the subarchnoid space, peridural anesthesia was used with good results. General anesthesia with ether is indicated for version and is also recommended for short operations. The author claims advantages for cyclopropane and advises against the use of nitrous oxide for long periods because it leads to dangerous anoxemia of the fetus; with cyclopropane, anoxemia does not develop, as so much oxygen has to be used with it. When cyclopropane is not available, ether should be used with nitrous oxide induction. In cesarean section, extraction by forceps or the management of normal labor when episiotomy is necessary, local infiltration is recommended as an efficacious method which offers no danger for mother and child.

J. P. GREENHILL.

Magalhaes, D.: *Continuous Caudal Analgesia of Hingson and Edwards*, *Rev. de ginec. e d'obst.* 37: 221-250, 1943.

The author is the first in Brazil to report the results of this method which was used in 10 labors. In general, the results were satisfactory and encouraging. The

total duration of labor was shortened: the first and third stages were shorter, while the second was greatly facilitated and could also be of shorter duration if intelligently controlled.

There was one fetal death which, from the results of the autopsy, could not be attributed to the technique of the analgesia. In another case, intervention was necessary because of fetal suffering. The intervention consisted of a high application of forceps in a primipara. The author thinks that such a dangerous operation could never have been crowned with the success it had, if there had not been absolute relaxation of the soft tissues given by the technique of analgesia which facilitated his work to the highest degree.

J. P. GREENHILL.

Leon, J.: *Obstetric Analgesia With Barbiturates*, *Semana méd.* 1: 1260-1263, 1943.

The author reiterates results in a previously published study which he feels has been misinterpreted by others, and restates his opinion regarding the efficacy of barbiturates in obstetrics. Only 30.5 per cent of patients experienced complete analgesia and amnesia, without any complications. These represented the optimal results obtained. The remaining cases were divided into six groups, according to whether the analgesic-amnesic effect was complete, but accompanied by untoward effects; or whether it was relative. The worst results were represented by two cases in which there was no analgesic or amnesic effect, but toxic symptoms.

Although barbiturates certainly do not constitute a panacea for relief of pain in all obstetric cases, the author believes that results obtained with these preparations are no worse than with other drugs used for this purpose. On the contrary, satisfactory results are being obtained, particularly when barbiturates are combined with gas anesthesia.

His final conclusions, cited from his previous paper, are: The most satisfactory procedure for relief of pain from the beginning of labor consists in utilizing in the waiting period a sedative—antispasmodic or hypoanalgesic—for amnesia, whose choice will depend on various clinical and obstetric conditions; and in the period of expulsion, gases or regional anesthesia. It is difficult, actually, to admit that a single method exists, adaptable in a standard, routine form to all circumstances, and so it is necessary to proceed in this, as in all clinical problems, with eclectic acumen, choosing the method, in each case, which, from careful examination, appears most useful.

J. P. GREENHILL.

Levine, W., Herzlich, J., Halperin, J., and Taller, H.: *Continuous Caudal Anesthesia in Obstetrics*, *Am. J. Surg.* 64: 31, 1944.

Continuous caudal anesthesia was used in a series of 250 cases. The authors claim good results including no untoward effects upon the newborn infants that could be attributed to the anesthesia, diminution in blood loss, greatly facilitated operative procedures, and marked shortening of the first stage of labor. Several women showed mild circulatory disturbances which were easily combated. It is interesting to note that 2 cesarean sections were performed under this form of anesthesia without incident.

FRANK SPIELMAN.

Hanley, B. J.: *Obstetrical Analgesia in Private Patients*, *Am. J. Surg.* 54: 403, 1941.

A series of 312 private cases are reported in whom nembutal and scopolamine were used to induce analgesia. Good results were obtained in 82 per cent. Most of the patients who failed to respond were in hard labor before the analgesia was begun so

that there was insufficient time for the drugs to induce sleep. There were no maternal complications which could be attributed to the analgesia, and only one baby was stillborn due to a prolapsed cord. Twelve babies showed signs of asphyxia, but all responded to the introduction of a tracheal catheter and/or carbogen inhalations. The author emphasizes that although the combination of nembutal and scopolamine (in dosage of 6 grains and $\frac{1}{150}$ grain respectively) is safe, the patients so treated require constant supervision. The length of the first stage of labor is not increased, but the lack of cooperation from the patient during the second stage increases the incidence of outlet forceps.

FRANK SPIELMAN.

Burton, Harold: Low Spinal Anesthesia During Labor in Cases of Cardiac Failure, *Brit. M. J.* 4316: 389, 1943.

The author repudiates cesarean section in cardiaes. He advocates natural delivery or low forceps under low spinal anesthesia using 0.6 c.c. of heavy procaine injected between the third and fourth lumbar vertebrae.

He has demonstrated the relative safety of this procedure in over 100 normal cases, and cites two illustrative cases of marked cardiac disease in which this form of anesthesia was used to alleviate pain and to eliminate the "bearing down" reflex.

He mentions headache as a complicating symptom which may persist as long as a week.

FRED L. ADAIR.

Guttman, Samuel A.: Demerol, *J. A. M. A.* 124: 155, 1944.

Observations are made in patients with intracranial lesions. These patients received 100 mg. of demerol parenterally. Seven of the 20 cases had a respiratory rate depression below the safe level (12 or less per minute). Instances of contracted pupils with sluggish response to light were observed.

WILLIAM BERMAN.

Gallen, Bedelia, and Prescott, Frederick: Pethidine as an Obstetric Analgesic, *Brit. M. J.* 4335: 176, 1944.

The pharmacology of the drug is reviewed. In the dosage employed, pethidine was an effective analgesic. It did not produce amnesia unless given with adequate doses of either barbiturates or scopolamine. Only 5 per cent of the patients failed to obtain any relief from pethidine. Analgesia was complete or satisfactory in 60 per cent. When given intravenously, it produces analgesia in 5 to 10 minutes, and when given intramuscularly, it takes effect in about 15 minutes. The duration of action is 3 to 4 hours. Intravenous administration is contraindicated in labor complicated by toxemia or hypertension. It has a definite antispasmodic action on the cervix. It prolonged labor somewhat, but there was no increase in the incidence of instrumental deliveries. Reactions in the mother included vomiting, dizziness, tingling of the limbs, and dryness of the throat. These symptoms were transient. Nine per cent of the babies so born needed resuscitation.

WILLIAM BERMAN.

Malignancies

Pineda, Julio y Porres: Papillary Adenocarcinoma of the Ovary, *Rev. méd. cubana* 55: 186-191, 1944.

Papillary adenocarcinoma of the ovary is discussed, with a case report by the author. This is the most frequent type of malignant tumor of the ovary and

shows the least satisfactory postoperative results. Only about 15 per cent of patients survive more than five years. Prognosis is largely dependent on the grade of malignancy. Statistics show that in grade 1 adenocarcinomas, the five-year survival rate is about 38 per cent and about 27 per cent in the pseudomucinous type, as compared with 4 per cent and 0 per cent respectively in grade 2 and grade 3 adenocarcinoma.

Radiotherapy is also an important factor. In comparing a series of 82 patients in which some received postoperative irradiation and others did not, 42 per cent of those irradiated with adequate dosage survived five years, and only 32 per cent of those who did not receive radiotherapy. Only 9 per cent who received inadequate radiation treatment lived five years after operation.

Nevertheless, operation yields the best results and should be carried out in every case. Only actual observation and subsequent histopathologic study of tissue permits an accurate prognosis. Later irradiation also increases the survival rate.

J. P. GREENHILL.

Dominguez, R., Sisco, R., Zamora Perez, and Agüero, O.: Hydatiform Mole Treated by Abdominal Hysterotomy, *Rev. de gynec. e d'obst.* 3: 139-145, Nov. 3, 1943.

The authors report a case in a woman 22, with symptoms of hemorrhage and hypogastric pain. In this case, high intervention was chosen, because of the patient's serious condition and the fact that the condition of the cervix indicated that dilatation and curettage would be unsuccessful. The authors believe, however, that Schumann's abdominal hysterotomy technique should be the exception, and never could be justified as a routine procedure in these cases. There are definite indications for its use in exceptional cases such as the one reported, in which operation by the vaginal route would entail too much risk.

J. P. GREENHILL.

Nestarez, O. B., and Franco, S. C.: Subarachnoid Alcohol Injections in the Treatment of Genital Neoplasms, *An. brasil. de ginec.* 17: 173-184, 1944.

The authors review the various measures used to relieve intractable pain in genital cancer including rhizotomy, cordotomy, pelvic sympathectomy, paravertebral alcohol injections, subarachnoid ammonium sulfate injections and the used opium alkaloids. The authors were particularly interested in subarachnoid alcohol injections, and they discuss the type of pain relief from all aspects such as physiology and rationale, indications, contraindications, technique, physical behavior of the alcohol in the spinal fluid, complications, etc. They used alcohol injections in 16 cases of cancer of the cervix where intractable pain was present, and they employed Stern's technique. The results were good in 7, and fair in 3. The complications observed were urinary retention in 3 cases, and paralysis of right leg in 1 case. The patients survived from 1 to 6 months.

J. P. GREENHILL.

Fels, E.: Treatment of Cancer of the Breast With Male Sex Hormone, *Semana méd.* 51: 166-170, 1944.

A preliminary report on three cases is presented by the author. Testosterone propionate was the preparation used. All three patients had advanced lesions. In the first two, these were recurrent, with metastases, despite surgical and radiologic treatment. The third patient refused operation but had radium treatment for a deep ulcerating lesion in an advanced stage. Satisfactory results were not to be

hoped for in any of these patients, yet all displayed relief of symptoms after receiving testosterone propionate.

J. P. GREENHILL.

Tuchschmid, G.: Chorionepitheliomas: Two Cases With Negative Aschheim-Zondek Reactions, Schweiz. med. Wchnschr. 73: 1493-1495, 1943.

It has already been pointed out that it is possible to have a negative Aschheim-Zondek test in the presence of an hydatid mole or a chorionepithelioma. Hence, in clinically doubtful cases, a curettement should be carried out in spite of the negative test. Thus far the cases reported have been hydatid moles or metastases of chorionepithelioma. The two cases reported by Tuchschmid were instances of primary chorionepithelioma of the uterus. In the first case, the neoplasm involved the entire uterine wall to the serosa, yet the biologic test was negative for both the urine and the blood. Such cases cannot be explained by Aschheim's assumption that the negative test in some cases of hydatid mole is due to long retention of the mole.

J. P. GREENHILL.

Horta, G.: Wertheim's Operation in Cancer of the Cervix, Rev. de gynec. e d'obst. 37: 172-176, 1943.

The author states that the absence of radium and of apparatus for deep roentgen therapy at the hospital of his city imposes recourse to surgery as effective or palliative treatment of cancer of the cervix. Preference goes to Wertheim's operation because the hypogastric lymph nodes are involved in 20 per cent of tumors strictly limited to the cervix and in 50 per cent of those in which the parametrium is slightly infiltrated.

Of 142 cases, 26 were of grade 1, 35 of grade 2, 31 of grade 3, 23 of grade 4, and 27 were not classified because of insufficient description of the gynecologic examination. Eighty cases were inoperable, 8 patients refused operation and 54 were submitted to Wertheim's operation. The latter included 19 cases of grade 1, 21 of grade 2, 2 of grade 3, 6 of grade 4 and 6 unclassified ones.

Fifteen patients died of operative complications, a mortality rate of 27.7 per cent. Eleven patients survived without signs of local or distant recurrence for from 1 to 13.5 years (six survived five or more years). Fourteen patients died of various causes, including recurrence and metastasis, from a few days to four years after operation.

J. P. GREENHILL.

Otken, L. B.: Primary Melanotic Sarcoma of the Ovary, Am. J. Surg. 55: 160, 1942.

According to the author, a careful review of the literature reveals only 6 cases of true primary melanotic sarcoma of the ovary, although many reports of metastatic melanotic tumors are to be found. He now adds a seventh case occurring in a 33-year-old white nulligravida. Her symptoms consisted of lower abdominal pain and menorrhagia of at least 1 year in duration. At the time of admission to the hospital, the symptoms and signs were those of a twisted ovarian cyst. At operation, bilateral hemorrhagic ovarian neoplasms were found, the left twisted, necessitating the removal of the uterus, tubes, and ovaries. Sections from the tumor were submitted to 3 competent pathologists all of whom concurred in the diagnosis. There were no metastases, and examination 3 months after operation failed to show any evidence of recurrence.

FRANK SPIELMAN.

Cesarean Section

Dubrovsky, R.: Dynamics of the Uterus as an Indication for Cesarean Section, *Obst. y ginec. latino-am.* 2: 22-37, 1944.

Dubrovsky analyzed the cesarean sections which were performed solely for disturbances in uterine action in the Buenos Aires Maternity Institute. There were only 34 such cases, and the small number is due to the conservatism practiced in the author's hospital. If there is no progress in the cervix after ten hours of labor, the author says the obstetrician is justified in performing a cesarean section. The indications for the operation were as follows: cervical spasm and hypertonicity 44.1 per cent, primary hypertonicity 23 per cent, mixed types 14 per cent, etc. In most of the cases, the patient had been in labor more than twenty hours and the bag of waters had been ruptured at least ten hours. Various types of cesarean section were performed. The maternal mortality was 5.9 per cent and there were no fetal deaths.

J. P. GREENHILL.

Leon, J.: Modern Abdominal Cesarean Section, *Rev. Oral de Cienc Med.* 8: Sept. 30, 1943.

The author traces the evolution of the operation and states that the advent of intraperitoneal sulfonamide therapy constitutes a positive advance, but that it is not yet known whether it will allow the transperitoneal cervical cesarean section to be performed safely even in infected women. In the meantime, if the transperitoneal technique is used, all efforts must be made to avoid primary and secondary contamination of the peritoneum even in women with apparently satisfactory conditions of ovular aseptis.

There is no doubt that the defensive techniques contribute to the amelioration of the prognosis in impure cases. Conditions are not as favorable for the use of an intraperitoneal Mikulicz as they are in gynecologic operations, because the puerperal uterus changes its position, form and dimensions. But a gauze drain or tube applied to the muscular wall of the lower segment is certainly useful as a complement of most artificially extraperitoneal cesarean procedures.

At present, intrauterine and intraperitoneal sulfonamide therapy is indicated in transperitoneal and artificially extraperitoneal cesarean sections, and the drug should be continued orally or parenterally, or through an abdominal drainage tube during the subsequent days.

In the cervical cesarean section, the author recommends a curved incision with concavity facing upward, because it offers a number of advantages. He prefers this technique transperitoneally in pure cases; in impure ones, he used his artificial extraperitoneal method of fixation of impermeable pads to the edges of the visceral peritoneum), and sulfonamide therapy with both techniques. Up till now, there has been no maternal mortality.

J. P. GREENHILL.

Vickers, D. M.: Cesarean Section, *Am. J. Surg.* 63: 168, 1944.

One hundred cesarean sections, in a series of 2,192 deliveries performed at a rural hospital in New York State, are reported, an incidence of 4.4 per cent. There was no maternal mortality, but 12 fetal deaths included 4 stillbirths and 8 in the neonatal period. The type of operation used in all cases was low classical with reflexion of the bladder peritoneum, low vertical uterine incision, and only partial peritonealization of the latter by means of the bladder flap. Indications and contraindications for operation are discussed, and the importance of early operation, when indicated, stressed.

FRANK SPIELMAN.

Endocrinology

Von Wattenwyl, H.: A New Method of Administering Estrogenic Substances, *Schweiz. med. Wchnschr.* 74: 159, 1944.

A few years ago Freed and Greenhill employed aqueous suspensions of estrone to overcome the disadvantages of implanting pellets of estrogenic substance used for the purpose of relieving symptoms of the menopause. The encouraging results obtained by means of this procedure led Wattenwyl to try it at the Basel Woman's Clinic. Among the sixteen women treated, the distressing menopausal symptoms began in 7 after a natural menopause, in 6 after operative castration and in 3 after irradiation of the ovaries. The patients were relieved of their distress by means of the aqueous suspensions and in order to rule out psychic influences, the author performed endometrial biopsies in 3 cases. In two he found distinct evidence of proliferation. The author agrees with Freed and Greenhill that aqueous suspensions give more marked relief than equal amounts of estradiol dipropionate in oil, but they did not observe a prolonged effect. They admit, however, that the rate of absorption of the hormone depends not on the aqueous medicine, but on the type of hormone used and the form and size of the crystals.

J. P. GREENHILL.

Schuermann, F.: Hormone Therapy of Postclimacteric Hearing Disturbances in Women, *Schweiz. med. Wchnschr.* 74: 1944, 1944.

The author selected a group of twenty women between 40 and 61 years, all of whom were in the menopause. In all, the complaint was increased hearing disturbances, roaring sounds and pressure sensation in the ears following the climacteric. By administering injections of 5 mg. of estrogen intramuscularly a number of times, the disagreeable symptoms were relieved but the hearing was not improved.

J. P. GREENHILL.

Powell, Tracy O.: The Lymphatics of the Female Urinary Bladder, *Surg., Gynec. & Obst.* 78: 605, 1944.

The lymphatic drainage of the female urinary bladder was studied by means of injection of the submucosa with India ink. For this problem, human cadavers were used. As a general rule, the lymphatic network was found to begin in the submucosa and progress laterally to either side. Here, they joined larger collecting vessels which contained valves. The lymphatics of the anterior wall join the large lateral collectors which in turn run down along the course of the obliterated hypogastric arteries toward the bladder neck. They then turn laterally to the primary nodes. Unlike these, the collectors of the posterior wall progress separately to the regional nodes. The large network of lymphatics around the neck of the bladder connects with those of the posterior wall and also the cervical lymphatics. While there are few anastomoses between the lymph vessels of the anterior wall across the midline, such junctions abound on the posterior wall. The posterior abdominal lymph nodes drain not only the bladder but the other pelvic organs as well.

L. M. HELLMAN.

Correspondence

Therapeutic Abortion

To the Editor:

The recently published paper by Drs. Cosgrove and Carter entitled "A Consideration of Therapeutic Abortion" has interested and puzzled me a great deal. The incidence of therapeutic abortion which they cited for the Johns Hopkins Hospital, namely, 1 to 35 deliveries, is precisely correct for the particular year chosen, 1941 to 1942. The implication is, of course, that this figure is representative of the practice in this department. Being rather startled to find our clinic with the unenviable distinction of topping the list—indeed, of far exceeding all the other clinics mentioned in the incidence of the operation, I have reviewed the figures in our yearly reports since 1927 (the first year such a report was issued). The results are shown in the accompanying table, which brings out two main facts.

TABLE I

THE INCIDENCE OF THERAPEUTIC ABORTION AT THE JOHNS HOPKINS HOSPITAL, 1927 TO 1944. UP TO 1942, THE PERIOD COVERED BY EACH YEAR DESIGNATED WAS A TWELVE-MONTH INTERVAL ENDING AUGUST 31 OF THAT YEAR. THE STATISTICS WERE PUT ON THE BASIS OF THE CALENDAR YEAR IN 1943

| YEAR | THERAPEUTIC ABORTIONS | DELIVERIES | PER CENT DELIVERIES | RATIO | |
|-------|--------------------------|------------|------------------------|-------|-----------------------------|
| 1927 | 13 | 1,114 | 1.2 | 1:860 | Ratio 1927 to 1935 |
| 1928 | 6 | 1,094 | 0.5 | 1:182 | |
| 1929 | 7 | 1,033 | 0.7 | 1:148 | |
| 1930 | 22 | 1,120 | 2.0 | 1:510 | |
| 1931 | 32 | 1,053 | 3.0 | 1:330 | |
| 1932 | 27 | 1,120 | 2.4 | 1:410 | Ratio 1936 to 1944 |
| 1933 | 20 | 1,193 | 1.7 | 1:600 | |
| 1934 | 31 | 1,224 | 2.5 | 1:390 | |
| 1935 | 28 | 1,216 | 2.3 | 1:430 | |
| 1936 | 23 | 1,583 | 1.5 | 1:690 | |
| 1937 | 26 | 1,645 | 1.6 | 1:630 | Ratio 1936 to 1944 |
| 1938 | 12 | 1,935 | 0.6 | 1:161 | |
| 1939 | 38 | 1,876 | 2.0 | 1:490 | |
| 1940 | 24 | 1,831 | 1.3 | 1:760 | |
| 1941 | 29 | 1,704 | 1.7 | 1:590 | |
| 1942 | 55 | 1,903 | 2.9 | 1:350 | 1:65 |
| 1942* | 8 | 700 | 1.1 | 1:880 | |
| 1943 | 18 | 1,880 | 1.0 | 1:104 | |
| 1944† | 18 | 1,341 | 1.3 | 1:740 | |
| Total | 437 | 26,565 | 1.6 | 1:610 | |

*Four-month period ending 12/31/42.

†First nine months.

The fact that our incidence of therapeutic abortion during the past decade or so is about one-half the figure cited is probably of minor importance, because even with a ratio of 1:65 we still lead the list and still remain about as far away as ever from the almost astronomical figure of 1:16,750 at the Margaret Hague Maternity.

The second fact shown by the table is this: Throughout the eighteen-year period covered, although there have been marked fluctuations from year to year, the incidence has been about the same for any given period provided a sufficient number of years are grouped to avoid sampling errors. Thus, in the first nine-year period shown, the frequency was 1 to 55 and during the second nine years,

1 to 65. This holds true despite the fact that the clinic has had three department heads over the eighteen-year interval (J. W. Williams, 1927 to 1931; J. M. Bergland, 1932 to 1936; myself since 1936). Now, it is rather hard for me to believe that the obstetric conscience of all three of us should differ from that of Dr. Cosgrove as widely as the tremendous difference in figures would indicate, and I have been groping for an explanation.

My chief quandary is this: How in the world can one practice good obstetrics (and I do know that the practice of obstetrics at the Margaret Hague Maternity is excellent) with a therapeutic abortion rate of only 1 to 16,750 deliveries? If an incidence of 1 to 500 was cited, or even 1 to 1,000, I would have regarded the report with envy and esteem, but 1 to 16,750 leaves me bewildered.

A slight suggestion of an answer to my query presented itself in connection with the three cases of severe hypertensive, vasculorenal disease which were not aborted. Only three cases of severe hypertensive vasculorenal disease in 67,000 deliveries! For some reason or another we see every year, in less than 2,000 deliveries, five or six comparable patients, each with fresh retinal hemorrhages and growing exudates in addition. And, is it possible that in the vast series there has not been a single case of carcinoma of the cervix complicating an early pregnancy? Nor a single early pregnancy in a woman with known rheumatic heart disease and a history of recent cardiac failure? After thinking the problem over, about the only conclusion I can reach is that cases of this sort, and similar ones in which "the imminence of lethal risk to the mother" is incontrovertible, rarely reach the Margaret Hague Maternity. Can it possibly be that the views stated in this article, have been so thoroughly voiced in Jersey City over the years that cases requiring interruption are referred elsewhere?

If there be any truth in the thought expressed in the foregoing paragraph, it follows as a natural sequence that some other hospital or hospitals in Jersey City will receive for consideration a disproportionately large number of cases in which therapeutic abortion is indicated. Even though that hospital may follow rigid criteria in determining the necessity for interference in this referred material, its incidence of therapeutic abortion will be high if judged by average statistics or the statistics of clinics which tend to sidestep the unpleasant responsibility of such cases. Local circumstances and prejudices play a most important role in this problem of incidence. Certainly, here in Maryland they represent probably the chief factor in the frequency of therapeutic abortion in the various hospitals.

One other point deserves consideration. The presentation in question emphasizes fetal wastage but ignores the ultimate maternal mortality which is implicit in too rigorously withholding therapy. Indications for therapeutic abortion must be based upon experience with the risks which threaten the lives of sick pregnant women. No obstetrician of integrity advocates departure from such indications, but in stressing the necessity of strict standards, it must not be forgotten that reduction in maternal mortality is still the paramount aim of modern obstetrics.

BALTIMORE, Md.
OCTOBER 5, 1944.

NICHOLSON J. EASTMAN, M.D.

Reply by Dr. Cosgrove

To the Editor:

In reply to Dr. Eastman, I desire to comment as follows:

First, please believe there was no invidious purpose in having picked out a particular year which showed this incidence of therapeutic abortions especially high. In all the figures quoted, I strove to get the most recent figures available, so as to reflect current practice. Had we had an incidence which made possible a compilation of our figures in relation to similar short periods, I would have reported ours on that basis. But it is perfectly obvious why I could not do this.

I stated specifically in my paper that I did not in the least desire to sit in judgment on other men's conscientious acts, nor to question the conscience of any individual. Certainly no one would dare to impugn the high ideals and conscience of men like Profs. Williams, and Bergland and Dr. Eastman. My effort was to establish a common criterion for the application of conscientious activities, and by quoting our broad experience, to perhaps rid men's minds of what I believe are in many cases "bugaboos" in the mental approach to the relation between obstetrics and other conditions. In this connection, it is entirely possible that concepts accepted by Dr. Williams many years ago may have influenced the thought in his clinic through all the years since.

The fact that we only aborted three cases of vasculorenal disease does not at all mean that those were the only cases of this condition we have seen in our material. It merely means that our attitude even toward these very ominous cases is perhaps different from that of other clinics. I attempted some discussion of this attitude in my paper.

We do seem, in this community, curiously, to see relatively few carcinomata of the cervix in childbearing women. I have checked this matter in the experience of several of the most competent and active members of our staff, in relation to their very large private material. However, the fact that we would not abort them, that is, attempt emptying the uterus as a special, separate procedure, does not at all mean we would withhold proper treatment of such cases. We would subject them to irradiation or extirpation of the uterus, or any combination of such measures judged best in the individual case, without regard to the presence of a conceptus in the diseased uterus. This because we think this is better treatment than the prior or simultaneous employment of surgery to empty the uterus. Even the spontaneous expulsion of the conceptus through the diseased cervix is a less dangerous trauma than, for instance, hysterotomy.

Of course, we have seen numbers of cases of known rheumatic heart disease, some of them with history of recent failure, or in actual failure when seen. Here again, our attitude is that abortion is not a justifiable procedure to apply to these cases. Instead we place great emphasis on adequate medical treatment of these conditions, believing that we are justified in our experience in concluding that if the medical control and treatment are adequate, the pregnancy may be virtually ignored except as emphasizing the stringency of medical control necessary.

Dr. Eastman's belief that a disproportionate number of cases legitimately necessitating therapeutic abortion are diverted to other institutions in the territory of the Margaret Hague Maternity Hospital by reason of the known attitudes of our own staff, is of course one which immediately occurs to the mind of anyone considering the local situation, and I have been at some pains to ascertain how far this may be true.

In a period during which this hospital delivered over 7,000 living births, there were 4,292 living births in other institutions in the county, the same area served by the Margaret Hague Maternity Hospital. Among these 4,292 living births, I have been able to obtain a record of only four therapeutic abortions, two for diabetes, one for tuberculosis and one for pyelonephritis. This is a rate of one in 1,073, definitely higher than our own published rate, but still by no means high enough to give credence to the belief that the other hospitals in this community practice therapeutic abortion in a disproportionate ratio.

Of course there are two unrecognized hospitals in this area, both small, where the incidence of abortion might well be in higher ratio than is consistent with any standard of good practice. These hospitals, however, are not attended by such men of good conscience as we like to think of ourselves being, and therefore, the work done therein would be quite beyond the pale of our discussion. Undoubtedly, such institutions also exist in other representative communities.

I will by no means plead guilty to inclusion in those "clinics which tend to sidestep the unpleasant responsibility of such cases." This clinic has never re-

fused to care for *any* case presented to it, nor transferred any case to another institution in an effort to sidestep *anything* unpleasant in relation to care of material coming to it. There are a number of men on this staff, including myself, who have done therapeutic abortions, and would have no hesitation whatever in inducing abortion if they honestly believed it necessary. I am glad to say that these men, with one possible exception, concur in the belief that the ultraconservatism of this clinic in relation to therapeutic abortion is good obstetrics.

One further point I would take issue on. Dr. Eastman states we ignore "the ultimate maternal mortality which is implicit in too rigorously withholding therapy." We do not ignore what is called the ultimate maternal mortality. But we do feel that this is a factor difficult to calculate, and that it may be conserved at least as well by additional emphasis on the medical treatment of complicating conditions, as by resort to a procedure that does utterly ignore the inherent right to life of human beings.

It occurs to me that there is perhaps one great difference in the experience of our two clinics. Johns Hopkins is eminently a referral and consultation center for a large area of the country. Ours serves only a relatively limited locality. The graduates of Johns Hopkins look to it for help in their own problems, and refer their own difficulties for solution on a relatively tremendous scale. It is probably true that many of his most difficult problem cases come to Dr. Eastman's service from more or less great distances. Inasmuch as this is true, it may very well be that he has an overload of those cases concerning which individuals superficially as different as he and myself in our approach to them, might conceivably get much closer together in our consideration of those particular cases.

Finally, I think that the work and results of this clinic sufficiently attest that we are alert to the reduction of maternal mortality as the paramount aim of modern obstetrics. As society realizes increasingly the necessity for adequate medical care of handicapped obstetric patients of every sort, the closer we will be to the possibility of staying true to that paramount aim, and, at the same time, of applying stricter standards than we have heretofore been able to, in respecting the rights of the unborn.

S. A. COSGROVE, M.D.

JERSEY CITY, N. J.

OCTOBER 30, 1944.

Is Abortion Murder?

To the Editor:

In an article entitled "A Consideration of Therapeutic Abortion" and published in the September, 1944, issue of the JOURNAL, the author employs the word "murder" in describing the procedure. Now in my belief, murder is an unpleasant and ugly word. His definition of murder: premeditated destruction of human life, is excellent as far as it goes, but it does not go far enough. One word is needed for completion, namely, malice. Because he has incorporated the word premeditated in definition, one would imply that destruction of human life is not murder unless it is premeditated, and I merely call attention to the fact that the premeditation must be with malice. I substantiate my viewpoint with definitions from Webster's International Dictionary.

Murder—n—The offense of killing a human being with malice, pretense, or aforethought, express or implied; intentional and unlawful homicide.

Murder—v—To kill with premeditated malice; to kill (a human being) willfully, deliberately and unlawfully.

Manslaughter—(law) The unlawful killing of a man, either in negligence or incidentally to the commission of some unlawful act, but without specific malice, or upon a sudden excitement of anger.

Homicide—(hom o man—caedere to cut) The killing of one human being by another. Homicide is of three kinds: justifiably, as when the killing is performed in the exercise of a right or performance of a duty; excusable, as when

done although not as a duty or right, yet without culpable or criminal intent; and felonious or involving what the law terms malice; the latter may be either manslaughter or murder.

Because of the incomplete definition, I believe Dr. Cosgrove has been led somewhat astray. What frequently is spoken of as murder and justifiable murder is not murder at all, as no malice is involved, either according to law or the conscience of the individual. It is homicide.

PITTSFIELD, MASS.

OCTOBER 4, 1944.

T. W. JONES, M.D.

Reply by Dr. Cosgrove

To the Editor:

In response to the above letter from Dr. Jones, I desire to comment as follows:

I am pleased that my article elicited your interest sufficiently to inspire so painstaking a commentary, and appreciate your expressing your enjoyment of it.

Of course "murder is an unpleasant and ugly word." That is one reason that I deliberately used it, to arrest attention and provoke serious thought. And, of course, I had not failed to familiarize myself with all the definitions quoted by Dr. Jones before using it.

But, in cognizance of all that he says as to its meaning, and granting that in the destruction of the previable fetus the operator is not actuated by *personal* malice ("enmity of heart; malevolence; ill-will"), yet that destruction can hardly be conceived to be activated by charity toward the creature destroyed.

In extension of this thought, part of Dr. Jones' own quoted definition says that the word murder used as a noun is, "The offense of killing a human being with malice, pretense, or aforethought, express or implied."

Please note the last word of that quotation; the "malice" need only be implied. This qualification is illuminated by part of the definition of malice according to the same dictionary on which you rely, as follows: "Malice, n . . . 4. *Law* . . . legal malice . . . does not necessarily consist in *malice in fact*, or actual malevolence toward the person injured . . . it may consist in *implied malice*, that is . . . wanton disregard of the rights of others."

Therefore, murder may in some cases be adequately defined as the premeditated killing of a human being with wanton disregard of the rights of the victim. So defined, I consider my use of the word murder to designate the destruction of a fetus to be entirely justified.

SAMUEL A. COSGROVE, M.D.

JERSEY CITY, N. J.

OCTOBER 16, 1944.

Postgraduate Education for Returning War Doctors*

To the Editor:

The receipt of an inquiry from the American Board of Obstetrics and Gynecology regarding the assignment, work, and disposition of Diplomates by the Armed Forces is further reassuring evidence of the group's interest in the integrity and improvement of the specialty, and implies a desire to aid the younger men who have been temporarily detached from orthodox practice and training.

It is evident that the Medical Bureaus of the various services have devoted much time and thought to the disposition of Medical Officers. The discrepancies are rare and are usually temporary. This is truly remarkable when the enormity, exactness, and grimness of the business of waging this war is considered; where a functioning doctor is the prime need and desire is necessarily secondary. It is

*The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

logical that the men in this specialty wished general duty, since the dependent clinics and Women's Corps constitute the only billet for such special work. The services are serious in their desire that the men be assured that their families will be cared for through regular private arrangements when practicable. Soon the gynecologically and/or obstetrically trained officers meet with only mild hilarity the frequent interrogation, "Who in the Army and/or Navy is going to have a baby?" It is the military counterpart of the compelling perennial of "never having lost a father."

It is right that the Board should be concerned about the potential and avowed candidates who were preparing for this specialty. The training that allowed the specialist to carry on the duties of a Medical Officer should be reciprocal, certainly in the foundation. It is unnecessary to recall the similarity in problems of hemorrhage, shock, infection, prophylaxis, and various medical and surgical complications regardless of the type of practice. These men are familiar with morbid processes.

In talking with these younger men, one is impressed with their eagerness to complete their formal training. The first information they seek is that concerning opportunities that might be available for them after the war. They are proud of the sacrifice that the institutions have made and of the splendid manner in which they have maintained their professional integrity during trying times and would be most reluctant to see the training standards lowered. There is no desire to take the place of the regularly appointed residents who were called away. The simple question is, "Will it be possible to secure an association with recognized groups where information and methods can be brought up to date, with possible recognition by the Boards?"

One who has attended the meetings of the two national societies, the Obstetric Congress, the various sectional groups, and the sections of the larger general associations is constantly impressed by the spontaneous and genuine interest of these leaders in the younger men and their eagerness to assist in the training. In all probability, measures have already been initiated by these groups and it is anticipated that the so-called "G-I Bill of Rights" will be a help, however, this is not generally known by the men in detached stations.

In a recent communication from Dean Davison, of Duke University Medical School, the writer was not surprised to hear that plans are being considered to aid men who desire Pediatric training. The plan would easily be applicable in obstetrics and gynecology throughout the United States. North Carolina is a "rural" state, has three medical schools that live in relative harmony. The men stick to their specialty, good hospital facilities are available, and the majority of the recognized specialists are Board members. The medical schools would receive and evaluate the applications, assign the applicants to the participating institutions and specialists, and the faculty's members would aid in the instruction if needed. The men could be rotated and brought together at intervals. The matter of costs, etc., could be agreed upon. This one plan, and it could easily be the wrong one, suggests the possibility of exercising the grand American prerogative of appointing a committee, which sometimes leads to definitive action.

The returning Medical Officers are used to a fairly rugged life. Many have not participated in competitive practice. Their way of living is adjusted to a fixed income and, except during combat, their work and rest are regulated. Under such circumstances it is easily understood why many will be content to work for some agency. The usual interest and manifest altruism of the splendid societies previously mentioned should adequately prove the advantage of the system of medicine as generally practiced throughout America. The postwar transition probably will not be so difficult and can be accomplished with few dislocations.

ROBERT A. ROSS,
COMMANDER (MC) USNR.

Items

Urology Award

The American Urological Association offers an annual award "not to exceed \$500" for an essay (or essays) on the result of some specific clinical or laboratory research in urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the Secretary, for full particulars.

The selected essay (or essays) will appear on the program of the forthcoming June meeting of the American Urological Association.

Essays must be in the hands of the Secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee, on or before March 15, 1945.

American Board of Obstetrics and Gynecology

Examinations

The next written examination and review of case histories (Part I) for candidates will be held in various cities of the United States and Canada and by special arrangements at Army and Navy Stations on Saturday, February 3, 1945, at 2:00 P.M. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year. All applications for this year's examinations must be in the office of the Secretary by November 15, 1944.

Arrangements will be made so far as is possible for candidates in Military Service to take the Part I examination (written paper and submission of case records) at their places of duty, the written examination to be proctored by the Commanding Officer (medical), or by a Medical Officer designated by him. Material for the written examination will be sent to the proctor several weeks in advance of the examination date. Candidates in Military Service who wish to do so may send their case records in advance of the examination date to the office of the Secretary. All other candidates should present their case records to the examiner at the time and place of taking the written examination.

The Office of the Surgeon General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may be ordered to Detached Duty for the purpose of taking these examinations whenever possible. The Office of the Surgeon General of the U. S. Navy presumably takes a similar attitude on this matter.

The place of the Board's Part II examination in May or June, 1945, has not yet been decided, but it is likely to be held in that city nearest to the largest group of candidates. The exact time and place will be announced later.

If a candidate in Service finds it impossible to proceed with the examinations of the Board, so that his plans are thus interrupted, deferment of parts of these without time penalty will be granted under a waiver of our published regulations covering civilian candidates.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS, M.D.

OCTOBER 19, 1944.

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